

# 2 Encephalopathy

---

*Wendy L. Wright*

## Encephalopathy and Delirium

- ◆ Encephalopathy is an acute confusional state that is accompanied by an alteration in the level of consciousness (drowsiness, stupor, or coma)
  - The term often used interchangeably with delirium
- ◆ Delirium is an acute, fluctuating state of confusion resulting from diffuse or multifocal cerebral dysfunction
  - Delirium is characterized by impaired attention, concentration, orientation, and memory, fluctuations of consciousness, disordered thinking, hallucinations, incoherent speech, and agitation
  - “Loud” delirium: hallucinations and psychomotor agitation
  - “Quiet” delirium: decreased mental acuity and inattention. This is less easily recognized than “loud” delirium but probably equally dangerous. Most common form in the elderly
- ◆ Avoid the notion of “intensive care unit (ICU) psychosis”; implies that encephalopathy is a consequence of the ICU stay and promotes complacency that may slow the search for all reversible precipitants
  - Encephalopathy in the ICU patient is a reflection of underlying illness or fatigue, *NOT* a result of being in the ICU
- ◆ “Sundowning” is often used to describe a delirium that develops in an elderly (usually demented) patient at night with disturbed sleep–wake cycle; again, promotes complacency, so avoid
- ◆ Impact of encephalopathy: increased length of ICU stay, increased mortality, prolonged mechanical ventilation, and increased risk of self-injury (e.g., self-extubation, pulling supporting catheters)

## Risk Factors

- ◆ Patients in an ICU are at high risk for encephalopathy because of:
  - Multisystem illnesses and comorbidities
  - Use of psychoactive medications
  - Advanced age
  - Malnutrition

## Evaluation

- ◆ ABCs: assess adequacy of airway, breathing, and circulation
  - Vital signs: look for tachycardia, hypotension, and hypoxemia
  - Arterial blood gas (ABG): look for failure of oxygenation or ventilation
- ◆ History
- ◆ Physical examination
- ◆ Labs
  - Glucose
  - Toxicology screen
  - Urinalysis
    - Rule out infection
    - Urine porphobilinogens in selected cases when porphyria is suspected
  - Complete blood count (CBC)
  - Electrolytes (including  $\text{Ca}^{++}$ ,  $\text{Mg}^{++}$ )
  - Liver function tests, serum ammonia
  - Blood cultures
  - Thyroid function tests
- ◆ Diagnostic studies
  - Chest x-ray
  - Head computed tomography (CT)
  - Lumbar puncture (LP)
  - Electroencephalogram (EEG)
- ◆ Avoid sedation

## Delirium Scales

- ◆ Need a monitoring and assessment device
- ◆ Many require a verbally responsive patient
- ◆ Intensive Care Delirium Screening checklist developed recently
  - Based on the presence of eight items
    - Altered level of consciousness
    - Inattention
    - Disorientation

- Hallucination or delusions
- Psychomotor agitation or retardation
- Inappropriate mood or speech
- Sleep–wake cycle disturbance
- Symptom fluctuation
- A score of four items on this scale has 99% sensitivity and 64% specificity when used to screen for delirium
- ◆ Confusion Assessment Method (CAM)-ICU
  - Has four features, the evaluation of which can be adapted if the patient is mechanically ventilated. Delirium is present if the patient has both features 1 and 2, and either feature 3 or 4
    1. An acute onset of mental status changes or fluctuating course
    2. Inattention
    3. Disorganized thinking
    4. An altered level of consciousness

## **Differentiating Features of Encephalopathy, Delirium, and Dementia**

- ◆ Dementia is a progressive disease involving disturbances in multiple spheres of cognition and not usually associated with a decreased level of consciousness early on
- ◆ Demented patients are more susceptible to developing encephalopathy

## **Treatment**

- ◆ Focus on determining and treating underlying cause
  - Rapidly reversible causes: treatment
    - Wernicke's encephalopathy: thiamine, glucose
    - Opiate induced: Naloxone
    - Benzodiazepine induced: Flumazenil
  - Modification of environmental factors
    - Allow uninterrupted sleep as often as possible
    - Room with a window or a well-lit room
    - Close observation with frequent redirection and reorientation
- ◆ Symptomatic Treatment
  - May be considered when available and not contraindicated
  - Define goals of treatment (i.e., reduce risk of self-injury, reduce tachycardia, patient comfort)
  - Haldol: PO/IV/IM in small doses, titrated for effect
    - Risk of extrapyramidal side effects and paradoxical agitation
    - Can take up to 10 min to work

- Can worsen delirium in alcohol withdrawal and cocaine-induced encephalopathy. Benzodiazepines are the treatment of choice in these cases
- Sedatives should be avoided if possible
- Midazolam can be used if the patient is at risk of injuring self but repeated doses should be avoided
- If restraints are used for patient safety they should be adjusted and checked periodically to prevent excessive constriction.

## **Causes and Management of Specific Causes of Encephalopathy**

- ♦ Mild systemic illness commonly produces encephalopathy in elderly or demented patients, especially when combined with new medications, fever, or sleep deprivation
- ♦ In the neurocritical care unit causes of altered mentation may be neurologic. Toxic and metabolic causes, however, should not be overlooked and often play a significant role in the neurocritical care setting
- ♦ Toxic
  - Medications commonly used in the ICU
    - Opiates as analgesics
    - $\text{MSO}_4$ , fentanyl, meperidine as epidural—rare cause of systemic toxicity
    - Benzodiazepines
    - Propofol
    - Steroids
  - Only in 5% of patients. Those who develop delirium often have an underlying affective or psychotic disorder
    - Acetylsalicylic acid
  - Neuroleptic malignant syndrome (*see* Chapter 4)
    - Encephalopathy, rigidity, hyperthermia, tachycardia, and hypertension are caused by neuroleptic medications such as haloperidol
    - Potentially fatal but can be treated with bromocriptine in mild cases, dantrolene in more severe cases
  - Industrial
    - Organophosphates
      - Symptoms: bradycardia, hypotension, miosis, increased lacrimation, nausea and/or vomiting, diarrhea, encephalopathy, seizures, and coma
      - Treatment: atropine, benzodiazepines, and phenytoin for seizures

- Carbon monoxide
  - Symptoms: Encephalopathy, dizziness, headache, tachycardia, ataxia, syncope and seizures
  - Treatment: 100% oxygen or hyperbaric oxygen
- Carbon disulfide
- Organic solvents
- Bromide
- Methyl chloride
- Heavy metals
  - Lead
  - Arsenic
  - Mercury
  - Bismuth
  - Thallium
  - Tin
- Environmental toxins
  - Plants and mushrooms
  - Venom (e.g., snakes, insects, fish)
- Inhalants
  - Gasoline
  - Glue
  - Ether
  - Nitrous oxide
  - Nitrates
- Illicit drugs
  - Cocaine
  - Heroin
  - Benzodiazepines
  - Lysergic Acid Diethylamide (LSD)
  - Phencyclidine (PCP)
- Withdrawal syndromes
  - Alcohol
    - ◇ Mild: Tremors, irritability, anorexia and nausea
      - Symptoms usually appear within a few hours after reduction or cessation of alcohol intake, and tend to resolve within 48 h
      - Symptoms may include dysphoria, insomnia, diaphoresis, impaired attention and concentration, tremors, and seizures
      - Tend to occur 1–10 d after cessation of benzodiazepines, may last several days to weeks

- ◇ Severe: “delirium tremens”—carries significant mortality
  - Tremulousness, hallucinations, agitation, confusion, disorientation, and autonomic hyperactivity (fever, tachycardia, and diaphoresis) typically occur 72–96 h after cessation of drinking
  - Symptoms generally resolve within 3–5 d.
- ◇ Alcohol withdrawal seizures: typically one or a few brief generalized convulsions
  - Occur 12–48 h after cessation of alcohol intake
  - Antiepileptic drugs are not indicated for typical alcohol withdrawal seizures
  - Other causes for seizures must be excluded
- ◇ Secondary derangements: patients with alcohol withdrawal are susceptible to hypomagnesemia, hypokalemia, hypoglycemia, and fluid losses, mostly as a result of fever, diaphoresis, and vomiting
- ◇ If hypoglycemia is present, thiamine should be administered before glucose to prevent precipitation of Wernicke’s encephalopathy
- ◇ Treatment
  - Chlordiazepoxide: 100 mg iv or PO q2–6 h as needed; Maximum dose: 500 mg in the first 24-h period. The initial 24-h dose can be administered again over the next 24 h, then the dosage can be reduced by 25–50mg per day each day thereafter
  - Lorazepam or other longer lasting benzodiazepines may facilitate smoother symptomatic control. Can be given 1–2 mg PO or IV q6–8 h as needed
  - Oxazepam 15–30 mg PO, q6–8 h as needed can be given to patients with hepatic failure, as it is excreted by the kidneys
  - Effective use of propofol drip has been reported.
  - Maintenance of fluid and electrolyte balance is important
  - Haloperidol should be avoided as it may cause paradoxical agitation
- Nicotine withdrawal
  - ◇ Signs and symptoms include bradycardia, depressed mood, anxiety, irritability, slowed cognition, sleep disruption, difficulty concentrating, increased appetite, and impatience

- ◊ Nicotine craving is most prominent within the first three days, and irritability, anxiety, and disturbed sleep peak at about 1 wk
- ◊ Treatment: 21 mg transdermal nicotine patch—anecdotal use in neurocritical care setting have not shown serious side effects
- ◆ Metabolic
  - Fluid disturbances
    - Dehydration: diabetes insipidus (DI), inadequate fluid administration
    - Water intoxication: psychogenic polydipsia, iatrogenic
  - Electrolyte disturbances
    - Hyponatremia
      - Causes: edematous states (CHF, nephritic syndrome, cirrhosis), endocrine dysfunction (hypothyroidism, adrenal insufficiency), iatrogenic (postoperative fluid overload, medication-induced, hypotonic fluid administration), SIADH, “cerebral salt wasting”
        - ◊ Post-op patients are at relatively high risk owing to stress, nausea, volume contraction, and medications
        - ◊ SIADH is a major cause in patients with CNS disease (brain abscess or infection, brain tumor, head trauma, etc.)
          - Treatment is by fluid restriction, unless the patient has vasospasm following subarachnoid hemorrhage, then hypertonic saline administration may be required
        - ◊ Centrally mediated renal sodium wasting (cerebral salt wasting)—existence of this syndrome is controversial
      - Results in cellular swelling and brain edema
      - Symptoms: weakness, confusion, disorientation, seizures, and coma
        - ◊ Rapidity of development is an important determinant of symptoms
      - Treatment
        - ◊ Can be conservative if hyponatremia developed gradually (also, often less symptomatic)
        - ◊ Balance risk of damage from hyponatremia vs risk of damage from central pontine myelinolysis
    - Hypernatremia
      - Causes: extrarenal (insensible losses owing to fever, burns, mechanical ventilation, diarrhea, and sweat), renal

- (osmotic diuresis, central DI, nephrogenic DI), iatrogenic (hypertonic saline administration, medications)
  - ◊ Typically will not develop if thirst mechanisms are intact and if there is unrestricted access and ability to drink water
  - Hyperosmolar state causes brain cells to shrink—brain equilibrates to these in several hours, therefore these states should be corrected slowly
  - Symptoms: agitation, seizures, lethargy, coma, and seizures; intracranial bleeding can develop as the shrinking brain pulls away from the meninges and bridging veins tear
- Glucose
  - Hypoglycemia
    - Confusion, seizures, stupor, coma, and occasionally hemiparesis or other focal neurologic findings
    - Typically caused by accidental or deliberate overdoses of insulin or antidiabetic agents, insulin-secreting islet cell tumors or retroperitoneal sarcoma, protracted ethanol intoxication (in rare cases)
    - Initial symptoms consist of nervousness, hunger, tachycardia, palpitations, anxiety, sweating, and tremor
      - ◊ Frequently recognized by the patient and respond quickly to oral or parenteral glucose
    - If the syndrome progresses, patients develop increasing confusion, drowsiness, motor restlessness, myoclonic twitching, and seizures
  - Hyperglycemia
    - Ketotic or non-ketotic
    - May lead to encephalopathy or coma
- Calcium: hypocalcemia, hypercalcemia
- Magnesium: hypomagnesemia, hypermagnesemia
- Respiratory
  - Hypoxia
  - Hypercapnia
    - Caused by underlying pulmonary disease or narcotic administration
    - CO<sub>2</sub> retention can cause headache, papilledema, and altered levels of consciousness
    - EEG frequently shows slowing in the theta and delta ranges
    - Hypercapnia usually does not cause prolonged coma or irreversible brain damage



- Treatment
    - ◇ Intermittent positive pressure ventilation
    - ◇ Oxygen can be dangerous because it may blunt the respiratory drive but should be administered to raise arterial oxygen tension to between 50 and 55 mmHg
  - Pulmonary embolus
- Infectious
  - Septic encephalopathy can be a result of any infections other than primary CNS infections
  - Symptoms may be owing to widespread multiorgan injury associated with the systemic inflammatory response
  - Causes of septic encephalopathy
    - Bacteremia/sepsis
    - Urinary tract infection/urosepsis
    - Pneumonia
    - Peritonitis
    - Bacterial endocarditis
- Gastrointestinal
  - Hepatic encephalopathy
    - Caused by cirrhosis of any cause, can be triggered or exacerbated by GI bleeding
    - EEG abnormalities can include bilaterally synchronous  $\delta$ -waves, that are frequently biphasic
    - Asterixis: lapses of sustained muscle contraction.  
Can occur with other metabolic encephalopathies as well (including hypercapnia)
    - Magnetic resonance imaging (MRI) can show diffuse cerebral edema
    - Ammonia levels are often elevated
    - Liver function tests can be high, low or normal
    - Coagulopathy can result
    - Treatment
      - ◇ Prevent elevated ammonia concentrations
      - ◇ Dietary restrictions of protein
      - ◇ Antibiotics (such as neomycin) to suppress or eliminate urease-producing bowel bacteria
      - ◇ Lactulose from 30 to 50 mL PO/rectally qd to qid
      - ◇ Liver transplant has been successful in reversing encephalopathy and even coma
  - Pancreatic insufficiency
- Renal failure leading to uremia

- Endocrine causes
  - Thyroid disease
    - Hypothyroidism
      - ◇ “Myxedema coma”: obtundation, nonpitting edema, hypothermia, hypoventilation, hypotension, and hypoglycemia
      - ◇ Treated with thyroid replacement with cardiovascular and pulmonary support; adrenal insufficiency may coexist
    - Hyperthyroidism
      - ◇ Encephalopathy, hyperdynamic cardiac function (tachycardia, increased cardiac output and ejection fraction), decreased vascular resistance, arrhythmias (afib, SVT), pulmonary compromise, and fever
      - ◇ If suspected, therapy should be started immediately. Close monitoring, cardiovascular/pulmonary/fluid support, and rapid administration of antithyroid drugs and  $\beta$ -blockers
  - Acute adrenal failure
    - Addisonian crisis from pituitary tumors, primary adrenal disease, adrenal suppression from chronic steroid therapy or rapid cessation of steroids
    - Symptoms: obtundation with hyponatremia and hyperkalemia
    - May follow infection, injury or surgery
    - Diagnosis can be confirmed by random cortisol levels below 20  $\mu\text{g/dL}$ ; if in doubt, a cosyntropin stimulation test may be required
    - Treatment: 100mg IV hydrocortisone followed by a 75–100 mg dose every 6 h, followed by an oral taper
      - ◇ If planning a cosyntropin test but immediate treatment is needed, give dexamethasone 4 mg iv every 4 h instead of hydrocortisone, as dexamethasone will not interfere with the measurement of endogenous cortisol levels; when the test is complete, the patient can be tapered to hydrocortisone
  - Hypopituitarism
    - Addison’s disease
    - Cushing’s disease
  - Parathyroid disorders
    - Hypoparathyroid
    - Hyperparathyroid

- Porphyria
- Nutritional
  - Vitamin deficiency
    - Thiamine
      - ◇ Wernicke's encephalopathy
      - ◇ Ophthalmoplegia, ataxia, global confusion
      - ◇ Treatment: immediate administration of thiamine 50–100 mg IV or IM. This dose should be repeated daily until the patient resumes a normal diet and should be given before glucose-containing solutions
      - ◇ Korsakoff's psychosis
    - B<sub>12</sub> deficiency
    - Folate deficiency
    - Pyridoxine deficiency
    - Nicotinic acid deficiency
  - Hypervitaminosis: A and D
- Body temperature: hypothermia, hyperthermia
- Acid-base disorders
- Cardiac: Arrhythmia
- Errors of metabolism
  - Wilson's disease

## Key Points

- ◆ Encephalopathy usually presents with nonfocal neurological exam as a result of diffuse cerebral disturbance
- ◆ Common and reversible etiologies should be investigated first (electrolytes, glucose, hypoxia, infection)
- ◆ Toxic and withdrawal syndromes occur commonly

## Suggested Reading

**American Psychiatric Association.** *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition. Washington, DC: American Psychiatric Association; 1994:123–133.

**Aminoff MJ, ed.** *Neurology and General Medicine*, 3rd edition. Philadelphia: Churchill Livingstone; 2001:593–615, 617–629, 631–644, 861–867, 1053–1067.

**Bergeron N, Dubois MJ, Dumont M, et al.** Intensive care delirium screening checklist: evaluation of a new screening tool. *Intensive Care Med* 2001;27:859–864.

**Bergeron N, Skrobik Y, and Dubois MJ.** (2002) Delirium in critically ill patients. *Crit Care* 2002;6(3):181–182.

- Chen R and Young GB.** Metabolic encephalopathies. *Baillieres Clin Neurol* 1996;5(3):577–598.
- Ely EW, Gautam S, Margolin R, et al.** The impact of delirium in the intensive care unit on hospital length of stay. *Intensive Care Medicine* 2001;27:1892–1900.
- Ely EW, Margolin R, Francis J, et al.** (2001) Evaluation of delirium in critically ill patients: validation of the confusion assessment method for the intensive care unit (CAM-ICU). *Crit Care Med* 2001;29(7): 1370–1379.
- Marino PL, ed.** *The ICU Book*, 2nd edition. Philadelphia: Lippincott, Williams and Wilkins;1998:779–793.
- Naik-Tolani S, Oropello JM, and Benjamin E.** (1999) Neurologic complications in the intensive care unit. *Clin Chest Med* 1999;20(2): 423–34, ix.
- Rincon HG, Granados M, Unutzer J, et al.** Prevalence, detection and treatment of anxiety, depression and delirium in the adult critical care unit. *Psychosomatics* 2001;42:391–396.

Handbook of Neurocritical Care

Bhardwaj, A.; Mirski, M.A.; Ulatowski, J.A.

2004, XVI, 337 p. 7 illus. With CD-ROM., Hardcover

ISBN: 978-1-58829-273-5

A product of Humana Press