

Toxic-Metabolic Encephalopathy



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KEYWORDS

• Encephalopathy • Delirium • Toxic-metabolic • Confusion • Altered mental status

HOSPITAL MEDICINE CLINICS CHECKLIST

1. Toxic-metabolic encephalopathy is an acute confusional state and is used interchangeably with the terms delirium and altered mental status.
2. The diagnosis of encephalopathy is based on clinical criteria with key features being fluctuations in level of awareness, attention, and cognition over a short period of time.
3. The pathophysiology for encephalopathy is currently unknown. However, neurotransmitter imbalance with cholinergic deficiency and dopamine excess are thought to play a role.
4. The history, examination, and basic investigations are useful in diagnosing an encephalopathy and identifying the underlying cause. Particular attention should be paid to medication changes.
5. Primary prevention is the most effective strategy to reduce cases of delirium.
6. Further management should focus on nonpharmacologic measures, including reorientation and close supervision. Restraints should be avoided.
7. Pharmacologic treatment may be required to ensure the safety of the patient and staff. Typical and atypical antipsychotics have efficacy in the treatment of delirium.

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DEFINITION

The term encephalopathy is derived from the Greek roots *encephalos* (brain) and *pathos* (suffering) to mean a general dysfunction of the brain. In the modern sense, encephalopathy is synonymous with an acute confusional state and is used interchangeably with delirium and altered mental status. There have been many proposed definitions for encephalopathy and delirium. The 5th edition of American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders defines delirium as fluctuating disturbance in attention and awareness.¹ Delirium is caused by an underlying physiologic disorder and is distinct from dementia in which confusion is caused by progressive neurodegeneration. The recently implemented International Classification of Diseases-10 coding defines delirium as a confusional state marked by impairment of attention and consciousness, global decrease in cognition, psychomotor disturbance, sleep-cycle alteration, and emotional disturbance.² Toxic-metabolic encephalopathy refers to the large subset of cases in which cognitive dysfunction is caused not by direct neural injury (such as strokes) but rather as a bystander effect from systemic medical illness, such as benzodiazepine drug effect, hyponatremia, or pneumonia.

EPIDEMIOLOGY

The prevalence of delirium varies in the setting. In general medical wards, 18% to 35% of patients are delirious.³ The rate is higher in intensive care units in which more than half of older adults are estimated to be delirious.⁴ On the other hand, in postacute care nursing home or rehabilitation, the prevalence of delirium is much lower at 14%.⁵ Aside from severity of illness, advanced age and prior cognitive impairment increase the risk for developing delirium.⁶ In addition, in about 40% of elderly patients, hospitalization is associated with reversible cognitive dysfunction: many of these cognitive symptoms, while not meeting criteria for delirium, indicate encephalopathy with systemic disease.⁷

PATHOPHYSIOLOGY

The pathophysiology of encephalopathy is unknown. There is no single cause, and encephalopathy is associated with many predisposing and precipitating factors (Table 1). Medications that alter neurotransmitter tone, such as diphenhydramine, can cause encephalopathy ("neurotransmitter hypothesis"). Particular attention has been paid to cholinergic deficiency because acetylcholine modulates attention, and patients with Alzheimer disease, which causes cholinergic loss, are at increased risk

Table 1
Factors in delirium

Predisposing	Precipitating
Dementia or cognitive impairment	Drugs: sedatives or psychoactive
Functional impairment	Use of physical restraints
Visual or hearing impairment	Use of bladder catheter
Depression	Laboratory abnormalities: physiologic stressors
History of transient ischemic attack or stroke	Infection
Alcohol misuse	Surgery
Older age (>65 y)	Iatrogenic event

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