

Intensive Care Unit Syndrome

A Dangerous Misnomer

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The terms *intensive care unit (ICU) syndrome* and *ICU psychosis* have been used interchangeably to describe a cluster of psychiatric symptoms that are unique to the ICU environment. It is often postulated that aspects of the ICU, such as sleep deprivation and sensory overload or monotony, are causes of the syndrome. This article reviews the empirical support for these propositions. We conclude that ICU syndrome does not differ from delirium and that ICU syndrome is caused exclusively by organic stressors on the central nervous system. We argue further that the term *ICU syndrome* is dangerous because it impedes standardized communication and research and may reduce the vigilance necessary to promptly investigate and reverse the medical cause of the delirium. Directions for future research are suggested. *Arch Intern Med.* 2000;160:906-909

Numerous authors have noted a cluster of psychiatric signs and symptoms that may occur in patients who are treated in an intensive care unit (ICU) or high-dependency ward and have termed this syndrome *ICU psychosis*,¹⁻³ *postoperative delirium*,⁴ and *ICU syndrome*;⁵ when patients have undergone heart surgery, it has been called *postcardiotomy delirium*⁶ or *cardiac psychosis*.⁷ Frequently, this syndrome is assumed to be peculiar to ICUs.

The aims of this article are to review the etiology and nature of this syndrome and then to discuss the implications of this review for nosology and management. Is there actually a psychiatric syndrome that is attributable to some feature of the ICU experience, or is this "syndrome" most accurately and most helpfully classified as a delirium? We argue that the latter is true and that it is possible and preferable to describe the disorder using established medical nomenclature. Appropriate classification will help to demystify the concept, ensure that crucial organic causes are sought and found, indicate optimal management, and facilitate standardized research.

CLINICAL FEATURES

Several authors have described the features of ICU syndrome, and while there are

inconsistencies in the way the syndrome is described, the suggested hallmark signs are a fluctuating level of consciousness, poor orientation, delusions and hallucinations, and behavioral anomalies, such as aggression or passivity.^{1,3,5} The ICU syndrome, as usually described, has a rapid onset and is transient, lasting only 24 to 48 hours,⁸ although a longer average duration of 14.7 days has been reported.⁹ These features are consistent with the diagnosis of delirium. The remainder of this article is devoted to delirium in the ICU setting, unless the term *ICU syndrome* is specified.

Delirium is clearly described in both the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*,¹⁰ and the *International Classification of Diseases, 10th Revision*,¹¹ which represent the major classification systems applying to psychiatry. In both, delirium is said to feature a disturbance of consciousness and attention; a change in cognition or perceptual disturbances, such as hallucinations; a rapid onset; and the assumption of an underlying medical cause.

The average incidence of postoperative delirium has been found to be approximately 40%,¹² although the incidence may vary according to the type of ICU or high-dependency ward. Some studies have demonstrated a consistent rate of underdiagnosis,^{13,14} so that the true incidence may exceed 40%. Delirium in the ICU is associated with longer admissions^{15,16} and increased mortality,^{15,17} although this may be a consequence of the

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underlying causative illness rather than delirium itself.¹⁷

In practice, with severely ill patients, making a formal diagnosis of delirium can be very difficult. In addition to delirium, a number of differential psychiatric diagnoses warrant consideration. A diagnosis of acute functional psychosis can only be made in the absence of a known medical cause of the symptoms. However, a diagnosis of psychosis on these grounds alone is dangerous and may simply reflect either that there has not been sufficient testing to identify the underlying medical cause¹⁵ or that the test results have normalized but the delirium continues (for example, in hyponatremia). Acute functional psychosis is best differentiated from delirium by consideration of the typical mental state findings in functional psychoses. In functional psychoses, global cognitive impairment is less frequent, consciousness remains clear and stable, and delusions are sustained and systematized.¹⁸ Dementia and delirium can be quite similar in presentation; moreover, delirium can be superimposed on dementia. Although patients with dementia (alone) have demonstrable cognitive deficits, they arise in clear consciousness.^{10,19} Dementia normally has an insidious onset and a stable course over short periods.

ETIOLOGY OF DELIRIUM IN THE ICU

The literature on the etiology of delirium in the ICU suggests a broad variety of causative factors. In addition to physiological disturbances, other causes suggested include psychological stressors, sleep deprivation, noise, and other environmental factors. The literature is critically reviewed below, paying particular attention to well-controlled studies rather than case reports or personal observations from clinicians.

Physiological Causes

The fundamental causal influences for delirium are medical factors and have been comprehensively reviewed elsewhere.^{18,19} These reviews have indicated that the most common factors include the following: metabolic disturbances, electrolyte imbalances, withdrawal syndromes, acute infec-

Class	Example
Anesthetic agents	Propofol Lidocaine (lignocaine) Bupivacaine hydrochloride
Analgesics	Fentanyl citrate Meperidine hydrochloride (pethidine) Morphine sulfate
Antibiotics	Penicillins Cephalosporins Tetracyclines (eg, doxycycline) Macrolides (eg, erythromycin) Quinolones (eg, ciprofloxacin) Aminoglycosides (eg, tobramycin) Monobactams (eg, aztreonam) Imidazoles (eg, metronidazole) Carbapenems (eg, imipenem)
Anticholinergics	Atropine
Antihypertensives	Tricyclic antidepressants Enalapril maleate Hydralazine Methyldopa Diltiazem Verapamil
Antiarrhythmics	Flecainide acetate Mexiletine hydrochloride
Anticonvulsants	Carbamazepine Clonazepam Phenobarbital (phenobarbitone) Phenytoin
H1 and H2 antagonists	Chlorpheniramine Famotidine Ranitidine Cimetidine
Others	Omeprazole

tion (intracranial and systemic), seizures, head trauma, vascular disorders, and intracranial space-occupying lesions. Many medications and substances cause delirium through intoxication or poisoning and withdrawal (**Table**). Murray¹⁹ has listed 90 therapeutic drugs that have been found to be associated with delirium. Tertiary-referral ICUs are more likely to have patients with multiorgan dysfunction, increasing the likelihood of development of delirium in these centers. Patients who have undergone cardiectomy have a unique set of iatrogenic factors contributing to the development of delirium.^{6,12} In less acute settings, most patients will have multiple contributors.¹⁷

Premorbid Cognitive Status

The only premorbid factors that have been reliably shown to predict delirium are prior cognitive level and age. It is argued that age disposes a patient to delirium through changes in pharma-

cokinetics and pharmacodynamics, reduced capacity for homeostatic regulation, and structural brain disease and physiological processes associated with aging.¹⁸ Several studies have demonstrated high correlations between pre-morbid cognition and postoperative confusion, disorientation, reduced consciousness, and even mortality.^{20,21}

Sleep Deprivation

Early research pointed to the role of sleep deprivation in causing ICU syndrome.²² Since then, despite contradictory research²³ and no clearly supportive empirical evidence, this notion has been perpetuated. A number of commentary or educational articles^{1-3,24} assert the role of sleep deprivation without reference to any primary research other than correlational studies.

There are a number of fundamental problems with correlational studies and other arguments that reduce the likelihood that sleep

deprivation does significantly contribute to delirium.

First, experimental studies on healthy adult volunteers have confirmed that rapid eye movement (REM) and total sleep deprivation can lead to some cognitive and perceptual changes, such as impaired concentration, disorientation, and visual disturbances.²⁵⁻²⁷ While perceptual anomalies may be experienced as hallucinations, they are frequently identified as such by the experimental subjects,²⁸ which is not the case in the patient with delirium, who will generally have poor insight into the hallucinations or delusions and may be very distressed by them.¹⁸ The effects of sleep deprivation on cognition and perception in humans do not mimic or even approach the gross and fluctuating cognitive impairment seen in delirium or ICU syndrome as described in the literature.²⁷

Second, it is not conclusive that the lack of sleep precedes (and therefore can cause) delirium. International diagnostic criteria list sleep disturbance as a necessary diagnostic symptom of delirium rather than being a cause of the disturbance.¹¹ One study demonstrated that insomnia followed the onset of delirium,²⁹ and another study similarly concluded that the inability to sleep and the inability to remain fully alert "were probably the result rather than the cause of cerebral dysfunction."³⁰

Third, a serious confounding factor in correlational studies is that the interruption of sleep has been found to correspond to the severity of a patient's medical condition.⁵ Thus, while any deterioration of mental state might be the result of sleep deprivation, it is just as likely to be the result of physical illness. No studies have adequately controlled for the severity of physical illness.

Fourth, not all correlational studies have found a relationship between sleep deprivation and acute confusion.²³ In their review of 80 primary-data studies of postoperative delirium, Dyer et al¹² concluded that lack of sleep was not a predisposing factor.

The ICU Environment

As with sleep, other environmental factors have frequently been cited as being causes of ICU syndrome with-

out due scrutiny of the empirical basis for this conclusion. Social isolation, immobilization, unfamiliar surroundings, excessive noise, and sensory monotony or absence of diurnal light variation have all been implicated. The ICU environment is replete with stress-inducing levels of noise, lighting, and movement. Several studies have documented that decibel levels in ICUs exceed the recommended normal levels.^{31,32} While these factors may place a degree of stress on a person, they are not documented causes of altered consciousness, delusions, or perceptual disturbances of the quality or severity seen in delirium,³³ nor are these factors necessary conditions for delirium to occur. With sufficient organic problems, a person will develop delirium regardless of the environment.

Psychological Factors

The thesis that psychological distress may cause a confused and delirious state has been tempting because the type and degree of stress on a patient in the ICU is remarkable.⁴ Patients are simultaneously subjected to a threat to life, the awe of medical procedures, an inability to communicate needs, a new and threatening environment, and the loss of personal control.

Early researchers studied preoperative psychological characteristics, including personality traits and coping styles. Later research has examined other psychosocial factors, such as marital distress, preoperative anxiety and depression, ambivalence about surgery, and history of psychosis. Dubin and colleagues³⁴ reviewed the literature on personality and psychological factors predisposing patients to postcardiotomy delirium,³⁴ and they highlight a number of serious methodological problems before concluding that there are no psychological correlates of delirium. They state that

no real personality profile has been developed that would allow one to predict postoperative outcome [and that] the postoperative medical state is the most important determinant in postoperative delirium.³⁴

Another review of the literature on postcardiotomy delirium concluded that there were no significant corre-

lations between delirium and any psychological or demographic factor.³⁵

In summary, published research strongly points to underlying medical problems, rather than environmental or psychosocial factors, as the primary cause of delirium in the ICU. The proposition that ICU syndrome is in fact a delirium has been articulated previously,^{36,37} yet the concept of a distinct ICU syndrome seems to persist in much of the peer-reviewed literature.

MANAGEMENT

The medical management of delirium is 2-fold: find and reverse the underlying medical problems and then control any behavioral disturbance, if applicable. Lipowski¹⁸ has summarized the core management requirement as follows:

Treatment should relate to both the cause and the symptoms of delirium. The underlying cause of the cerebral dysfunction needs to be removed whenever possible, or treated. Adequate fluid and electrolyte balance, nutrition and vitamin supply should be ensured.¹⁸

Many episodes of delirium have more than one medical cause, and any of these causes may perpetuate psychiatric disturbances. Appropriate investigations for the patient who is delirious postoperatively will include a complete blood cell count, biochemical screen, measurement of arterial blood gas levels, chest x-ray, and urine microbiological testing. Once disturbances are identified, they must promptly be reversed as far as possible. If behavioral disturbance jeopardizes management, temporary chemical sedation may be warranted. While recognizing its occasional potential for cardiovascular instability, haloperidol, 0.5 to 2.0 mg 1 to 4 times daily, appears to be accepted as the treatment of choice.^{38,39} Benzodiazepines should be avoided, except in the case of alcohol withdrawal, as they may perpetuate the delirium.¹⁹

In terms of the psychosocial and environmental management of delirium, the following suggestions have been cited in the literature: establish clear and normalized communication with the patient^{2,19}; reorient the patient to time and place frequently⁴⁰; and pro-

vide the patient with an environment conducive to sleep (ie, moderate noise) and adequate analgesia.² It has also been suggested that a preoperative psychological interview can help to prevent postoperative delirium,^{41,42} but this requires further research. It is important to note that while these management suggestions have some prima facie validity, there is no evidence from controlled trials to support their efficacy.

CONCLUSIONS

ICU syndrome is a term that has been used in the literature for over 30 years, surviving through a series of reports, very few of which are primary research articles.¹² The supposition that there are features intrinsic to the ICU environment that can cause a psychiatric syndrome has rarely been critically discussed. The current review indicates that ICU syndrome does not differ from delirium, a better-known and more widely researched nosological entity. The term *ICU syndrome* is not helpful and potentially dangerous, since it implies that some causes that are not organic are responsible, which may discourage thorough investigation and treatment of the medical causes. Unlike delirium, ICU syndrome is informally classified and inconsistently defined, and it is not an internationally accepted diagnostic term. The proper diagnosis of a disease should facilitate communication among colleagues and aid physicians in making a timely selection of the best treatment for that disease. Using the term *ICU syndrome* undermines both actions.

Delirium occurs in at least 40% of patients in high-dependency units and ICUs. Its hallmark features are a reduced level of consciousness, disturbed cognition (memory, orientation, and language), and perceptual disturbances, with rapid onset and a fluctuating course. The main causes are metabolic disturbances, electrolyte abnormalities, withdrawal or intoxication syndromes, acute infection, vascular disorders, or lesions in the central nervous system. There is no sound evidence that either sleep deprivation or the ICU environment can cause delirium. While these factors may lower the threshold for delirium in a medically ill person, this hypothesis has not been directly investigated. No person-

ality variables have been reliably associated with the development of delirium, and there is no good evidence for the role of psychological stress in its cause. Old age and premorbid cognitive dysfunction indicate a higher risk for the development of delirium.

We contend that ICU syndrome is an example of delirium and nothing more. Future research should be directed toward improving the identification, management, and prevention of delirium.

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