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Critical illness frequently is associated with neurologic failure that may involve the central and peripheral nervous systems. Central nervous system failure is associated with a spectrum of neuro-behavioral changes including delirium, coma, and long-term cognitive dysfunction. Peripheral neurologic failure, or critical illness neuromuscular abnormalities, is suggested by diffuse areflexic weakness and protracted respiratory insufficiency, and may also persist long after the acute hospitalization. While the burden of neurological disease complicating critical illness is considerable, preventive or therapeutic options are limited. This article provides an overview of research evaluating the relationship between critical illness and neurologic function, with a special emphasis on underlying mechanisms.

Coma After Global Ischemic Brain Injury: Pathophysiology and Emerging Therapies Robert E. Hoesch, Matthew A. Koenig, and Romergryko G. Geocadin	25
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Cardiac arrest is a major cause of death and morbidity in the United States, and neurological injury contributes significantly to this. Neurological complications associated with global cerebral ischemia include disorders of responsiveness, such as coma and the vegetative state, seizures, motor deficits, and brain death. Coma, complete unresponsiveness, is the most pervasive of these.

Therapies that improve neurological outcomes in general after cardiac arrest and therapies that stimulate arousal from coma could have enormous clinical impact. The authors review the physiology of arousal and describe the biochemical and pathophysiological derangements that develop after global cerebral ischemia. We then describe the potential therapeutic mechanisms of hypothermia and deep brain stimulation, which provide hope for better neurological outcomes after global cerebral ischemia.

Pathophysiology of Delirium in the Intensive Care Unit

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Max L. Gunther, Alessandro Morandi, and E. Wesley Ely

Delirium, or acute brain dysfunction, is a life-threatening global disturbance in cognitive functioning that frequently manifests in critically ill patients. This review examines the current status of knowledge regarding the pathophysiology of delirium in the ICU, in particular, evaluating the role of iatrogenic factors such as sedatives and analgesic administration in brain dysfunction. This hypothesis is considered along with several other plausible mechanisms of ICU delirium, including sepsis, postoperative cognitive dysfunction, and changes in biomarkers and neurotransmitters. The review concludes by highlighting potential future directions in molecular genetics for the elucidation of delirium and its long-term consequences.

The Encephalopathy in Sepsis

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Shidasp Siami, Djillali Annane, and Tarek Sharshar

Brain dysfunction is a severe complication of sepsis with an incidence ranging from 9% to 71% that is associated with increased morbidity and mortality. Its diagnosis relies mainly on neurologic examination with clinical manifestations ranging from confusion to coma. An electroencephalogram, somatosensory evoked potentials, and measurement of plasma S-100b protein and neuron-specific enolase can be useful for the detection of brain dysfunction. Brain MRI can identify brain lesions such as cerebral infarction, posterior reversible encephalopathy syndrome, and leukoencephalopathy. The mechanism of sepsis-associated encephalopathy involves inflammatory and non-inflammatory processes that affect endothelial cells, glial cells, and neurons and induce blood-brain barrier breakdown, derangements of intracellular metabolism, and cell death. Specific treatments for sepsis-associated encephalopathy need to be developed. Currently, treatment is mainly the management of sepsis.

Mechanisms of Cerebral Injury from Cardiac Surgery

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Charles W. Hogue, Rebecca F. Gottesman, and Joshua Stearns

Cerebral injury is a frequent complication of cardiac surgery, and it has been associated with high mortality, morbidity, hospital costs; an increased likelihood of admission to a secondary care facility

after hospital discharge; and impaired quality of life. This article examines postulated mechanisms for cerebral injury from cardiac surgery. Most emphasis has been placed in the past on the intraoperative interval as being the period of highest cerebral vulnerability. Many clinical cerebral events, however, occur in the postoperative period.

Brain Edema in Acute Liver Failure

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Andres T. Blei

Acute liver failure (ALF) is a syndrome of rapidly deteriorating liver function that manifests as coagulopathy and encephalopathy in a previously healthy individual. This article analyzes the repercussions of ALF on the brain through a discussion of special features of this syndrome, important for the interpretation of neurologic findings. Of particular interest within the context of ALF are hepatic encephalopathy and the pathogenesis of brain edema in acute liver failure as well as its clinical and therapeutic aspects.

Seizures and Status Epilepticus in the Critically Ill

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Marek A. Mirski and Panayiotis N. Varelas

Seizures represent stereotypic electroencephalographic (EEG) and behavioral paroxysms as a consequence of electrical neurologic derangement. Seizures are usually described as focal or generalized motor convulsions; however, nonconvulsive seizures that occur in the absence of motor activity may escape clinical detection. Because of the admission diagnoses and dramatic physiologic and metabolic derangements common to critically ill patients, the entire spectrum of seizure disorders may be encountered in the ICU. Seizures in the ICU are attributable to primary neurologic pathology or secondary to critical illness and clinical management. For optimal treatment, early diagnosis of the seizure type and its cause is important to ensure appropriate therapy. Convulsive status epilepticus requires emergent treatment before irreversible brain injury and severe metabolic disturbances occur.

The Alteration of Autonomic Function in Multiple Organ Dysfunction Syndrome

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Hendrik Schmidt, Dirk Hoyer, Joachim Wilhelm, Gerold Söffker, Konstantin Heinroth, Kuno Hottenrott, Samir M. Said, Michael Buerke, Ursula Müller-Werdan, and Karl Werdan

Autonomic dysfunction is associated with the severity of illness and mortality in patients with multiple organ dysfunction syndrome (MODS) and may contribute significantly to the pathogenesis of this syndrome. Several treatment approaches may possibly restore autonomic function in MODS and thus cause the survival benefit.

Mechanisms of Neuromuscular Dysfunction in Critical Illness 165
Jaffar Khan, Taylor B. Harrison, and Mark M. Rich

The development of neuromuscular dysfunction (NMD) during critical illness is increasingly recognized as a cause of failure to wean from mechanical ventilation and is associated with significant morbidity and mortality. At times, it is difficult to identify the presence of NMD and distinguish the etiology of the weakness in patients with critical illness, but subtle clinical findings and bedside electrophysiologic testing are helpful in establishing the diagnosis. This article describes the clinical spectrum of acquired neuromuscular weakness in the setting of critical illness, provides an approach to diagnosis, and discusses its pathogenesis. Finally, a defective sodium channel regulation as a unifying mechanism underlying NMD in critically ill patients is proposed.

The Pathophysiology of Long-term Neuromuscular and Cognitive Outcomes Following Critical Illness 179
Margaret S. Herridge, Jane Batt, and Ramona O. Hopkins

Despite the recent and marked improvement in short-term mortality after critical illness, significant morbidities persist for many patients following hospital discharge. This article discusses the risk factors for muscle, nerve, and brain dysfunction after critical illness and preliminary basic science data to support possible pathophysiologic mechanisms mediating this disability. Additionally, it presents a roadmap outlining future directions in this area of research.

Evidence-Based Performance and Quality Improvement in the Acute Cardiac Care Setting 201
Arthur L. Riba

This article was originally planned to appear in the October 2007 issue of Critical Care Clinics. The goal of this article is to summarize the indicators, processes, and dimensions of care that are linked to desired clinical outcomes of the most commonly encountered conditions in the acute cardiovascular care setting, and specifically, acute coronary syndromes and congestive heart failure. Additionally, it reinforces the concepts of best cardiovascular care practice and reviews some of the highly successful quality initiatives that have demonstrated a link between hospital process performance and outcomes. Particular attention is focused on the evidence-based treatments and diagnostic evaluation and processes of inpatient cardiovascular care, which lead to desired outcomes meaningful to patients and where available, provide physicians with the strategies and tools to be successful in translating scientific evidence into effective and rewarding care.

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