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Dane Nichols

Oxygen Delivery and Consumption: A Macrocirculatory Perspective	239
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Dane Nichols and Nathan D. Nielsen

Severe sepsis is a leading cause of death and resource use throughout the world. This article examines the relationship of oxygen delivery to oxygen use under varying conditions. Topics reviewed include the concept of the critical dissolved oxygen, concerns over shared measurement errors in obtaining estimates of oxygen consumption, seminal articles in this area, and the practice of early goal directed therapy.

Lactic Acidosis: Recognition, Kinetics, and Associated Prognosis	255
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Christopher Vernon and Jennifer L. LeTourneau

Lactic acidosis is a common condition encountered by critical care providers. Elevated lactate and decreased lactate clearance are important for prognostication. Not all lactate in the intensive care unit is due to tissue hypoxia or ischemia and other sources should be evaluated. Lactate, in and of itself, is unlikely to be harmful and is a preferred fuel for many cells. Treatment of lactic acidosis continues to be aimed the underlying source.

Mean Arterial Pressure: Therapeutic Goals and Pharmacologic Support	285
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David S. Shapiro and Laurie A. Loiacono

The Surviving Sepsis Campaign targets central venous pressure, mean arterial pressure, and central venous oxygen saturation as guides for resuscitation. Fluid resuscitation and the use of vasopressors are paramount to the success of the campaign's end points. Although the achievement of supranormal physiologic parameters has been associated with higher mortality in some studies, these slightly higher blood pressures may enable better oxygen delivery, in some observations. This article focuses on the mean arterial pressure goals during sepsis, the measurement of the mean arterial pressure, and the manipulation of this target with volume resuscitation and pharmacologic interventions.

Static Measures of Preload Assessment	295
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Richard A. Nahouraii and Susan E. Rowell

This article focuses on static methods for determining preload, specifically pressure and volumetric indices measured at the bedside. The underlying ventricular function will determine where the patient is located on Frank-Starling ventricular function curve and the patient's response to a fluid

challenge. The proper interpretation and use of such measures, coupled with an understanding of their limitations and knowledge of alternative methods, is necessary to guide properly volume resuscitation in the critically ill.

Dynamic Indices of Preload

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T. Miko Enomoto and Louise Harder

Hypotension and shock are important issues confronting the intensivist. Volume overload can have dire consequences such as decreased gas exchange and increased myocardial dysfunction. This article explores dynamic means of determining preload responsiveness.

Optimizing Hemodynamic Support in Septic Shock Using Central and Mixed Venous Oxygen Saturation

323

Supriya Maddirala and Akram Khan

Global tissue hypoxia is one of the most important factors in the development of multisystem organ dysfunction. In hemodynamically unstable critically ill patients, central venous oxygen saturation ($Scvo_2$) and mixed venous oxygen saturation (Svo_2) monitoring has been shown to be a better indicator of global tissue hypoxia than vital signs and other clinical parameters alone. Svo_2 is probably more representative of global tissue oxygenation, whereas $Scvo_2$, is less invasive. Svo_2 and $Scvo_2$ monitoring can have diagnostic and therapeutic uses in understanding the efficacy of interventions in treating critically ill, hemodynamically unstable patients.

The Optimal Hematocrit

335

Louise Harder and Lynn Boshkov

Nearly 15 million units of packed red blood cells and whole blood are transfused annually in the United States alone. Until recently, the major risks from blood transfusion were thought to be transmission of viral infections, and overall, blood transfusion was believed by most providers to be safe. A safe hemoglobin threshold above which red cell transfusion is clearly unnecessary has not been established. This article addresses the numerous problems that surround the use and consequences of blood transfusion, such as hemoglobin and hematocrit levels, oxygenation, storage time, immunomodulation, infection, and anemia. The relevant literature is comprehensively reviewed.

Techniques for Determining Cardiac Output in the Intensive Care Unit

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Imran Mohammed and Charles Phillips

To achieve the goals of resuscitation in critically ill patients, a thorough understanding of the techniques available to measure cardiac output is important. Recently the pulmonary artery catheter has fallen out of favor because of concerns of safety and a lack of efficacy. Newer less invasive techniques since have been developed and are gaining popularity. But is important to remember that the ability of these techniques to improve outcome has yet to be demonstrated, and one should apply caution in how they are used until their use in algorithmic treatment approaches have

been shown to improve outcome. This article discusses the invasive and noninvasive techniques to assess cardiac output.

The Role of Echocardiography in Hemodynamic Assessment of Septic Shock 365

Matthew J. Griffee, Matthias J. Merkel, and Kevin S. Wei

Echocardiography is a rapid, noninvasive, comprehensive cardiac assessment option for patients presenting with hemodynamic instability. In patients with septic shock, echocardiography can be used to guide fluid therapy by measuring collapsibility of the inferior vena cava. Sepsis-induced myocardial dysfunction can be diagnosed, and responses to therapy can be monitored with echo. Patients with persistent shock should be evaluated for right heart failure, dynamic left ventricular obstruction, or tamponade if they do not respond to resuscitation and norepinephrine. Unexpected or rare findings that affect management may be revealed using focused echocardiography. This article presents national and international competency statements regarding critical care echocardiography and training resources for intensivists.

Noninvasive Monitoring Cardiac Output Using Partial CO₂ Rebreathing 383

Brian P. Young and Lewis L. Low

This article reviews use of partial carbon dioxide rebreathing devices to determine cardiac output and their application for hemodynamic monitoring in the ICU and operating room. The primary focus is on the NICO monitoring device. Compared with conventional cardiac output methods, these techniques are noninvasive, easily automated, and provide real-time and continuous cardiac output monitoring. The advantages and limitations of each technique are different discussed.

Mechanisms, Detection, and Potential Management of Microcirculatory Disturbances in Sepsis 393

Imran Mohammed and Stephanie A. Nonas

Despite improvements in resuscitation and treatment of sepsis, the morbidity and mortality remain unacceptably high. Microvascular dysfunction has been shown to play a significant role in the pathogenesis of sepsis and is a potential new target in the management of sepsis. Clinical studies, aided by new techniques that allow for real-time assessment of the microcirculation, have shown that disturbances in microcirculatory flow are common in sepsis and correlate with worse outcomes. Bedside measurement of microcirculatory perfusion has become simpler and more accessible, and may provide key insights into prognosis in sepsis and guide future therapeutics, much like mean arterial pressure (MAP), lactate, and mixed central oxygen saturation (SvO₂) do now. The authors review here the role of microcirculatory dysfunction in sepsis and its potential role as a therapeutic target in sepsis.

Detection of Hypoxia at the Cellular Level

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Laurie A. Loiacono and David S. Shapiro

Organ function is critically linked to the way tissues use available oxygen. In sepsis, tissue-related hypoxic injury is the result of hypoxemia and hypoperfusion and cytokine-mediated mitochondrial dysfunction termed cytopathic hypoxia. Organ dysfunction in sepsis is more likely related to derailment of the metabolic processes of cells to use available oxygen. Cellular dysoxia rather than hypoxia may be the most appropriate way of describing sepsis-related tissue injury. Lactate is a marker of aerobic mitochondrial dysfunction and anaerobic tissue metabolism and in some circumstances is considered the fuel of choice for certain tissues. The concept of cellular metabolic derangement or cytopathic hypoxia as a potential cause for multiorgan system dysfunction in sepsis may direct efforts to optimize outcome in septic patients from the classic targets of CO, tissue perfusion, DV_{O_2} , and V_{O_2} toward moderating sepsis-related early cytokine response, maximizing mitochondrial function, and using biomarkers to monitor treatment response.

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