

## Reticulocyte Hemoglobin Content in Critically Ill Patients

To the Editor:

We read with interest the article by Fernandez *et al.*<sup>1</sup> Reticulocyte hemoglobin content (CHr) is a promising marker of iron metabolism, particularly in the intensive care unit setting where usual markers are often disrupted by inflammation. In a small cohort of critically ill patients with no evidence of real iron deficiency, we observed a correlation between C-reactive protein and CHr, suggesting that inflammation rapidly reduces iron availability for erythropoiesis.<sup>2</sup> We agree that CHr should be used in future research protocols to monitor the response to iron therapy in critically ill patients. However, CHr measurements are not routinely available in most hospitals. In our study, blood samples had to be stored on ice and sent to an external laboratory within 72 h.<sup>2</sup> In the study by Fernandez *et al.*,<sup>1</sup> it would have been interesting to know the iron status of the patients based on the ferritin concentration, serum iron concentration, and transferrin saturation to ensure that there was no coexistence of true iron deficiency. Also, because CHr is the product of cellular volume and cellular hemoglobin concentration, other variables such as mean cellular volume may have affected the CHr values.<sup>3,4</sup> In our study, two patients had a high CHr value ( $\geq 35$  pg) probably secondary to their high mean cellular volume values (more than 100 fl).<sup>2</sup> CHr seems to be useful to predict transfusions or to monitor iron therapy but should be interpreted in the context of folates or vitamin B<sub>12</sub> deficiencies that may coexist in critically ill patients.<sup>4,5</sup>

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The above letter was sent to the authors of the referenced report. The authors did not wish to reply. —James C. Eisenach, M.D., Editor-in-Chief.

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(Accepted for publication August 12, 2010.)

## From Creatine Kinase-MB to Troponin: Do We Really Need to Differentiate between Myocardial Injury and Infarction?

To the Editor:

We commend Archan *et al.*<sup>1</sup> for their excellent review on creatine kinase-MB fraction and troponin for the diagnosis of perioperative myocardial infarction (MI) in noncardiac surgery patients. We, too, recently investigated the utility of creatine kinase-MB and cardiac troponin I for predicting clinically relevant myocardial injury in two cohorts of patients who had undergone coronary artery bypass surgery (N = 1,576).<sup>2</sup> Similar to the studies the authors<sup>1</sup> reviewed, we also found cardiac troponin I to be superior to creatine kinase-MB in its association with increased hospital length of stay and mortality.<sup>2</sup>

When creating a universal definition for MI guidelines, the Joint European Society of Cardiology, American College of Cardiology, American Heart Association, and World Heart Federation Task Force identified five clinical classifications, although MI associated with coronary artery bypass surgery is the only category for perioperative MI.<sup>3</sup> From a mechanistic point of view, noncardiac surgical perioperative MI would likely be classified as a type 2 MI, “myocardial infarction secondary to ischemia due to either increased oxygen demand or decreased supply, for example coronary artery spasm, coronary embolism, anemia, arrhythmias, hypertension, or hypotension.”<sup>4</sup>

As Archan *et al.*<sup>1</sup> correctly note, the universal definition requires a combination of biomarker elevation and angina symptoms, electrocardiogram, imaging, or angiography to diagnose MI. This definition is problematic in the perioperative setting, however, because angina symptoms are not reliable in patients undergoing general anesthesia and receiving analgesics and sedatives. In addition, as a diagnostic tool, electrocardiogram is often not sensitive enough to detect ischemia—particularly after cardiac surgery.<sup>2</sup> Therefore,

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Supported by Research Starter Grant from the Society of Cardiovascular Anesthesiologists (Richmond, Virginia) (to Dr. Muehlschlegel), Mercedes Concepcion Faculty Development Fellowship Grant from the Department of Anesthesiology, Perioperative and Pain Medicine, Brigham and Women's Hospital (Boston, Massachusetts) (to Dr. Muehlschlegel), a grant from the National Institutes of Health (Bethesda, Maryland) (to Dr. Body), as well as institutional and/or departmental sources.

even in the absence of outcome data, we suggest using troponin as the primary criteria for identifying clinically significant myocardial injury in all perioperative settings.

We respectfully disagree with Archan *et al.*<sup>1</sup> regarding the relevance of differentiating between myocardial injury and myocardial infarction. They correctly point out that troponin elevation may result from a variety of etiologies, including physiologic stress associated with marathon running or mountain climbing.<sup>5</sup> Furthermore, the extraordinary sensitivity of currently available biomarker assays permits detection of a single troponin molecule release even after minimal exercise.<sup>6</sup> At present, however, imaging modalities and cellular detection technology are unable to differentiate between troponin release from the cytosol or damaged cells that are likely to recover (myocardial injury) and irreversible cellular necrosis (myocardial infarction). Therefore, we suggest that increased concentrations of circulating troponin, in fact, reflect a spectrum of myocardial injury. Consequently, the assignment of a specific cutoff point in an attempt to differentiate between injury and infarction may be counterproductive to efficient identification of therapeutic interventions.

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(Accepted for publication August 24, 2010.)

## On Memory, General Anesthesia, and Sleep

*To the Editor:*

I read with great interest the erudite editorial that accompanied the article by Pham *et al.*<sup>2</sup> by my colleague, Professor Lichtor.<sup>1</sup> In their article, Pham *et al.*<sup>2</sup> found no evidence of implicit memory formation during anesthesia in children.

Without providing clear and concise answers, Lichtor<sup>1</sup> asks the following question: *Is memory formation during anesthesia similar to what goes on during sleep?* General anesthesia abolishes explicit or conscious memory except in the rare cases of awareness during anesthesia.<sup>3</sup> The evidence for memory formation beyond unconsciousness is controversial. It may occur only during light anesthesia, short of consciousness.<sup>4</sup> When it occurs, there is only evidence of perceptual, but not conceptual, priming.<sup>5</sup> As for sleep, Lichtor<sup>1</sup> notes there is evidence that it contributes to the consolidation of some types of explicit memory. There are also some reports that it enhances the learning of motor and perceptual skills.<sup>6</sup>

Lichtor<sup>1</sup> asks another question: *Would patients have better postoperative control of pain and anxiety if therapeutic instructions are given both preoperatively and intraoperatively?* My answer has to be negative. For patients to comprehend instructions during anesthesia, there must be conceptual priming, which does not occur during anesthesia—except at its lightest levels (*e.g.*, nitrous oxide, opioids, and muscle relaxants),<sup>7</sup> where conscious encoding of stimuli is still possible.<sup>5</sup> After a 1988 report that claimed improved recovery and reduced hospital stay for patients after surgery,<sup>8</sup> nearly all credible and controlled studies failed to replicate this finding or other beneficial findings relating to postsurgical analgesia, nausea and vomiting, cessation of smoking, and so on.<sup>9</sup> The suggestion by Lichtor<sup>1</sup> that anesthesia might be similar to sleep processes that facilitate memory consolidation cannot be true because anesthetics abolish memory by *suppression* of consolidation.<sup>10-12</sup>

Finally, although Hermann Ebbinghaus introduced many important ideas and methods for memory research (with himself as the sole subject) in the late 19th century, I would attribute the introduction of implicit or nonconscious forms of human memory to the literature at a much later date. The first suggestion that conscious or implicit memory exists was in 1957, when Scoville and Milner reported the case of patient H.M., who after surgery for epilepsy was unable to convert a new short-term memory into a permanent long-

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