also critical in the care of patients with respiratory disorders or unbalanced pH and that these disorders cannot be evaluated with the use of pulse oximetry. In particular, a normal pulse oximetry measurement does not exclude important abnormalities in the partial pressure of arterial carbon dioxide (PaCO₂) or pH. Therefore, serious elevations in the PaCO₂, which are indicative of ventilatory dysfunction, can be present when the results of pulse oximetry are normal. Although noninvasive, transcutaneous CO₂ monitoring can be used to complement pulse oximetry, current technologies still require further development and are not indicative of acid–base status. Thus, clinicians need to be aware that levels of arterial and capillary blood gases remain a critical component of the evaluation of gas exchange.

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THE AUTHORS AND A COLLEAGUE REPLY: Avidan and Levin point out that the determination of hemoglobin concentrations for pulse oximetry are approximations. In the formulas shown in the video, we could have indicated that hemoglobin variables are estimates of the underlying true concentrations by inserting a tilde or a caret above the abbreviation for hemoglobin (Hb), but we made the decision to use a simplified approach to clarify the teaching point, as is done in many textbooks.

Even the reference measurement of SaO₂ in arterial blood performed by our institution’s blood gas laboratory involves the estimation of the relative concentrations of oxyhemoglobin and deoxyhemoglobin in an arterial blood sample with the use of infrared absorption co-oximetry. One can argue that all measurements are estimates and that the question of whether a particular monitoring technique constitutes a measurement or an estimate becomes semantic.

Regarding the inability of pulse oximetry to detect hypercarbia and metabolic disturbances, Man and Marsden bring up important points. Pulse oximetry is an excellent oxygenation monitor, but it does not alert the clinician to changes in ventilation in a timely manner, particularly when supplemental oxygen is used. Anesthesiologists are well aware of this limitation of pulse oximetry and recommend the use of capnography to monitor ventilation during procedural sedation.

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Since publication of their article, the authors report no further potential conflict of interest.

Case 10-2011: Fever, Confusion, and Liver Failure

TO THE EDITOR: With regard to the Case Record of a 60-year-old woman with fever, confusion, and liver failure (March 31 issue): we are interested in Tierney’s thoughts on the possibility that the combined use of pegylated interferon and ribavirin to treat the patient’s hepatitis C induced an autoimmune liver disease that contributed to her death.2,3 Her confusion and asterixis (suggesting hepatic encephalopathy), the markedly elevated levels of transaminases and the associated positive test result for autoimmune markers, and the response to glucocorticoids lead us to suspect a diagnosis of autoimmune liver disease. We are also curious as to whether the preexistence of cirrhosis affects the decision to include splenomegaly in the diagnostic criteria for hemophagocytic lymphohistiocytosis.

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TO THE EDITOR: Tierney et al. present the case of a woman with hemophagocytic lymphohistiocytosis who is treated with immunosuppressive therapy. Unfortunately, after an initial improvement, severe infectious complications developed that led to her death. Hemophagocytic syndrome is caused by the uncontrolled activation of macrophages and the release of proinflammatory cytokines (a cytokine storm). However, this activation concerns the macrophage-derived proinflammatory cytokines of the interleukin-1 family (interleukin-1α and 1β and interleukin-18), whereas levels of cytokines of the interleukin-1 family (interleukin-1α and 1β and interleukin-18), whereas levels of cytokines (so JIA): a report and review of the literature. Pediatr Rheumatol Online J 2005;3:79-85. (http://www.pedrheumonlinejournal.org/mar-ap%2005/pdf/case%20report%20-%20mas.pdf.)


The New England Journal of Medicine

No potential conflict of interest relevant to this letter was reported.

Eosinophil Granule Protein Localization in Eosinophilic Endomyocardial Disease

TO THE EDITOR: A 70-year-old man with chronic renal disease, splenomegaly, and eosinophilia presented with transient weakness in the left arm, visual disturbances, disequilibrium, and anomia. Magnetic resonance imaging of the brain showed findings consistent with numerous, small embolic strokes. Four echocardiograms, including a transesophageal echocardiogram, did not reveal abnormalities. Therapeutic trials of glucocorticoids and imatinib were unsuccessful at reducing the numbers of peripheral-blood eosinophils. To investigate the possibility that the emboli were the sequelae of eosinophilic endomyocardial disease, the patient underwent a biopsy of his right ventricle and intraventricular septum. Staining of the myocardium with hematoxylin and eosin did not show clinically significant abnormalities. Notably, only rare eosinophils were detected in the interstitium (Fig. 1A and 1B). However, immunohistologic examination with fluorescein-conjugated antibodies to eosinophil granule major basic protein 1 (MBP1) revealed striking extracellular deposits of eosinophil granule MBP1 (Fig. 1C and 1D). The eosinophil granule MBP1 was most prominent at apparent luminal surfaces, especially over an area of endocardium that stained most intensely.

Eosinophilic endomyocardial disease is a complication of the hypereosinophilic syndrome. A previous study showed eosinophil infiltration and deposition of toxic eosinophil granule proteins in damaged cardiac tissues. Netea et al. propose an elegant therapeutic alternative in anakinra, which offers the advantage of highly selective suppression of immune function and may minimize toxicity. The effects of treatment with anakinra are difficult to study since the number of adult patients with hemophagocytic lymphohistiocytosis is so small. The greater incidence in children, especially in Asia, which is quite often associated with Epstein–Barr virus infection, might make this fertile ground for such investigation, but it cannot be assumed that the pathogenesis in the pediatric and adult populations is similar. It is not clear whether the use of anakinra is applicable to both children and adults, but surely the idea is sound.

Sandoval suggests that the second patient mentioned in the case should be tested for mutations in SH2DIA and BIRC4, which may be associated with fatal infection with Epstein–Barr virus in young men. Genetic testing was performed before this patient died, and no mutations were found.

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