To the Editor: I read with interest a manuscript entitled “Monitoring of cerebral oxygenation during hypoxic gas management in congenital heart disease with increased pulmonary blood flow” by Takami and associates (1). I have some concerns about their conclusion that the systemic arterial oxygen saturation should be maintained greater than or equal to 80% in newborns with congenital heart disease and increased pulmonary blood flow.

The authors evaluate the method of treating patients with congenital heart disease and excessive pulmonary blood flow with supplemental nitrogen. This practice is based upon the premise that alveolar hypoxia may increase pulmonary vascular resistance and arterial hypoxemia may decrease systemic vascular resistance to improve the balance between pulmonary and systemic perfusion (2). They used near-infrared spectroscopy to measure changes in oxyhemoglobin, deoxyhemoglobin, total Hb, and tissue oxygenation index (TOI: oxyhemoglobin/total Hb). They found that TOI decreased when the oxygen saturation decreased. They inferred that cerebral tissue oxygenation likewise decreased.

It is essential to properly identify patients who may benefit from treatment with supplemental nitrogen. A target value for systemic oxygen saturation between 75% and 85% may be appropriate for patients with a functionally single ventricle or a common outlet from two ventricles. In appropriate patients with cyanotic congenital heart disease, supplemental nitrogen will decrease the ventricular volume load, and hopefully not compromise oxygen delivery to vital organs. This practice may actually improve oxygen delivery if a relatively high Hb level is maintained. Target values for systemic oxygen saturations between 75% and 85% are not appropriate for patients with two ventricles and a simple left-to-right shunt. These patients may have an appropriate balance in systemic and pulmonary blood flow with an oxygen saturation of 90% to 95%. In other words, it is not necessary, or appropriate, to create a net right-to-left shunt in patients with acyanotic congenital heart defects where there is no component of obligatory mixing between systemic and pulmonary venous return. It may have been appropriate for the authors to exclude 2 of the patients in this study with aortic arch obstruction.

The authors did not report the Hb measurements of patients. The change in TOI may have been influenced by the oxygen carrying capacity of the blood. The NIRO-300 can potentially measure changes in mitochondrial cytochrome aa3. It would be helpful to know if any changes in cytochrome aa3 were observed. If not, tissue oxygenation was potentially not impaired despite a decrease in TOI. Moreover, TOI is only the ratio of oxyhemoglobin and total Hb. It simply is not a measure of oxygen delivery. Cerebral perfusion may improve sufficiently to maintain adequate oxygen delivery despite a decrease in systemic oxygen saturation in patients with cyanotic congenital heart disease and excessive pulmonary blood flow when treated with supplemental nitrogen.

Takami and associates have reported important observations. I hope however, readers will consider the limitations of using TOI to describe cerebral oxygenation before they accept or reject the use of supplemental nitrogen in clinical practice. Additional research is needed to determine whether there are significant benefits or adverse effects from the use of supplemental nitrogen in patients with mixing lesions and excessive pulmonary blood flow.

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REFERENCES
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Response
To the Editor: We are very thankful for Dr. Day’s insightful comments and interest in our manuscript.

Initially, cytochrome aa3 (CytO2) was believed to be a very reliable indicator for reflecting the energy status of tissue. As Dr. Day pointed out, we believed that the measuring of cytochrome was effective when discussing oxygen delivery at the level of brain neurons. We conducted CytO2 measurements on all the infants in our study, but did not perform any follow-up examinations related to CytO2 because we were unable to produce any stable results, and recent research has not shown a reliability of CytO2. The manuscript did not include CytO2 data that could be used for estimating tissue oxygenation. As there have been various viewpoints concerning data on CytO2 from the past, the new model (NIRO-200) that has been provided by NIRS has been removed as a measurement item. At the moment, we believe that the tissue oxygenation index (TOI) is the most effective indicator for measuring the oxygenation of tissue.

We anticipated that oxygen delivery to tissue would be maintained because systemic and cerebral blood flow would increase, offsetting the decrease in oxygen saturation through hypoxic gas management. However, through this study, we