an inotropic agent after CPB. However, we hope some of the questions may be answered by the results of the TRICC study.

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Reply to the Editor:

We appreciate the interest of Haas and Camphausen in our recently published trial of triiodothyronine (T3) in neonatal heart surgery.¹ The points they raised are addressed below.

Our center, like many other centers performing infant heart surgery in the United States, routinely uses high-dose intravenous loop and thiazide diuretics rather than peritoneal dialysis to manage postoperative fluid overload. We agree that the results of our study cannot be generalized to patients who are treated with peritoneal dialysis.

The inotrope score used in our study, adapted from Wernovsky and associates,² was determined by the use of dopamine, dobutamine, milrinone, epinephrine, and norepinephrine. The cumulative dose of dopamine in particular did not differ between treatment groups during the first 5 days after the operation. Vasodilator use

was also similar between treatment groups: milrinone was used routinely in our patients, with no difference in cumulative milrinone dose between treatment arms at 5 days. A single patient (randomized to the T3 group) received nitroprusside; no patients received phenoxylbenzamine. Amiodarone was not used in any subject.

We planned our trial so that cardiac output was one of two primary outcome measures. The technique used (direct measurement of oxygen consumption by real-time gas exchange) provides an objective determination of cardiac output in children who are sedated, ventilated, and stable.³ During the study period, infants were weaned from mechanical ventilation at increasingly shorter times after surgery, rendering this measurement infeasible at 48 hours after surgery in several subjects. However, the proportion of patients in each treatment group in whom this end point could not be measured (9/22 in the T3 group and 5/20 in the placebo group) was not statistically significant ($P = .34$).

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A new modeling for each population To the Editor:

I read with great interest the recently published study by Fakler and associates¹ in the August 2005 issue of the *Journal*. They found, in their investigation, a poor agreement between the measured oxygen consumption (VO_2) and the VO_2 estimated using the formulas of Krovetz and Goldbloom² and LaFarge and Miettinen.³ According to the Krovetz-Goldbloom formula, the mean difference was -53 mL/min/m^2 and the limits of agreement were -95.5 and -11.1 mL/min/m^2 for the lower and upper limits, respectively. Use of the Krovetz-Goldbloom formula led to a systematic and significant overestimation in VO_2 values ($P = .0001$). However, a significant correlation was shown between measured and assumed VO_2 values with this formula ($R = .61$; $P = .0001$). According to the LaFarge-Miettinen formula, the mean difference was -15.6 mL/min/m^2 and the limits of agreement were -120.0 and 88.8 mL/min/m^2 for the lower and upper limits, respectively. A systematic and significant overestimation was also reported using the LaFarge-Miettinen formula. A significant correlation was, however, indicated between measured and assumed VO_2 with this model ($R = 0.38$; $P = .0037$). I speculated that the reason that the measured VO_2 values were significantly different from the assumed VO_2 using both Krovetz-Goldbloom and LaFarge-Miettinen formulas was because of a methodologic weakness in statistics and modeling.

As discussed by the authors, these differences between measured VO_2 and VO_2 estimated by the formulas might be due to a difference of population. I agree with this statement, but more credible is the argument that these differences are explained by the coefficients of these formulas (Krovetz-Goldbloom formula: $\text{VO}_2 = a \cdot \text{height} + b \cdot \text{weight} - c$; LaFarge-Miettinen formula: $\text{VO}_2 = a' - b' \cdot \ln(\text{age}) + c' \cdot \text{heart rate}$ for male subjects and $\text{VO}_2 = a' - b'' \cdot \ln(\text{age}) + c' \cdot \text{heart rate}$ for female subjects). These coefficients (a , b , c and a' , b' , b'' and c') depend on the characteristics of the population included in the study. That is why the use of published formulas without any coefficient correction cannot be applied in other populations, as shown in another study.⁴ To overcome this problem, new formulas with new coefficients should be calculated from the population

included in the investigation. For example, in the study of Fakler and associates,¹ new formulas with new coefficients could be calculated using 70 patients included in their investigation and could be validated against the remaining 73 patients for comparing measured and estimated VO_2 .

Fakler and associates¹ reported that the routine use of assumed VO_2 when calculating cardiac output with the direct Fick principle might frequently result in large errors in the estimation of cardiac output and dependent parameters. To obtain reliable cardiac output values by the direct Fick equation, VO_2 should be measured as concluded by Fakler and associates¹ or estimated with a new formula calculated using the population included in the study.

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Reply to the Editor:

We thank Benallal for his comments on our article and appreciate his remarks.

Our study was specifically designed to assess the importance of measured oxygen consumption (VO_2) in the preoperative diagnostic hemodynamic evaluation during cardiac catheterization and to assess whether published formulas allow a reliable calculation of VO_2 . We did not intend to develop a new formula to assume VO_2 .

Our results emphasize that both the Krovetz-Goldbloom formula,¹ which had been used to this point in our institution, and the more commonly used formula published by LaFarge and Miettinen² are not

feasible in all patients to assume VO_2 and thereby calculate cardiac output by the Fick principle.

Li and colleagues³ presented the important conclusion that other predictive equations published by Lundell and associates,⁴ Wessel and colleagues,⁵ and Lindahl⁶ also do not accurately estimate VO_2 . All these formulas were developed to offer a suitable and reliable method to assume VO_2 in order to simplify the calculation of hemodynamic parameters. However, these formulas cannot be used in all patients and settings.

As Benallal pointed out, these formulas include coefficients depending on characteristics of the population investigated in these studies. The difference between measured and assumed VO_2 might be due to a population difference. In addition, it is also influenced essentially by other conditions such as the mode of general anesthesia and relaxation used in different institutions.

It is difficult to identify feasible coefficients to develop a formula fitting to all conditions of hemodynamic evaluation during cardiac catheterization.

Moreover, we are convinced that our population of 143 patients is too small to identify and validate suitable coefficients for a new formula. LaFarge and Miettinen derived their most commonly used formulas from a multivariate analysis of covariance applied to data on a series of 879 patients.

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Linking gene expression, nuclear factor kappa B, remote ischemic preconditioning, and transplantation: A quest for an elusive Holy Grail or a road to an amazing discovery?

To the Editor:

We read with interest the recent paper of Ishiyama and colleagues¹ reporting that inhibition of nuclear factor kappa B (NF- κ B) by I κ B suppressor gene transfer ameliorated ischemia-reperfusion (IR) injury after experimental lung transplantation. A few comments seem appropriate.

Is activation of NF- κ B before transplantation destructive or protective? Two murine studies provided seemingly contradictory results. In the study of Ishiyama and colleagues,¹ inhibition of NF- κ B rendered protection against the IR injury, yet in another study² a targeted deletion of the p105 subunit of the NF- κ B abolished the protective effect of the remote ischemic preconditioning (rIPC), a novel clinically applicable mode of protection against IR injury, whereby the organs can be protected by a brief ischemia applied remotely (eg, limb ischemia). Gene expression appears to play an important role in rIPC. In our own studies, the rIPC stimulus modified NF- κ B regulated gene expression in leukocytes³ and the target organ,⁴ and when the rIPC was applied to the recipient in porcine model it rendered myocardial protection after the orthotopic heart transplantation.⁵

It is widely known that the transcription factor NF- κ B can be activated by a variety of stimuli, for example, tumor necrosis factor (TNF)- α , bacterial lipopolysaccharide (LPS), and heat shock protein (HSP). Stimulation of the cell may lead to phosphorylation of I κ B and translocation of NF- κ B into the nucleus, resulting in gene expression, including those genes responsible for exocytosis of adhesive molecules and cytokine production in leukocytes, but also for production of protective substances eg, manganese superoxide dismutase (Mn-SOD) and inducible nitric oxide synthase