method of "controlled reoxygenation," in which CPB is started with ambient Po_2 (30 mm Hg) and normoxic reoxygenation is begun at the time of cardioplegic arrest.⁴ Applying this method, we were able to avoid biochemical evidence of reoxygenation injury and to present almost complete functional recovery in previously hypoxic hearts.⁴

In normoxic adult hearts we demonstrated a beneficial effect in terms of enzyme release, polymorphonuclear leukocyte elastase production, and especially lipid peroxidation, by lowering oxygen levels (150 mm Hg) in the extracorporeal circuit⁵ (Fig. 1).

We were also able to show that treatment with oxygen-derived free radical scavengers can limit reoxygenation injury and avoid lipid peroxidation during CPB.⁶ I therefore partly agree with the authors, although we found convincing evidence that reduced Po_2 during CPB is more important and is indeed absolutely vital. Hyperoxia is not physiologic, it is damaging to all organs, and above all it is absolutely not necessary. I truly believe that within 5 to 10 years, CPB in hypoxic immature hearts, as well as in normoxic adult hearts, will be instituted only in a normoxic fashion to avoid oxygenation damage and lipid peroxidation.

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REFERENCES

1. Ihnken K, Morita K, Buckberg GD, Matheis G, Sherman MP, Allen BS, et al. Studies of hypoxemic/reoxygenation injury: without aortic clamping. II. Evidence for reoxygenation damage. *J Thorac Cardiovasc Surg* 1995;110:1171-81.
2. Morita K, Ihnken K, Buckberg GD, Sherman MP, Young HH. Studies of hypoxemic/reoxygenation injury: without aortic clamping. IX. Importance of avoiding perioperative hyperoxemia in the setting of previous cyanosis. *J Thorac Cardiovasc Surg* 1995;110:1235-44.
3. Ihnken K, Morita K, Buckberg GD, Young HH. Studies of hypoxemic/reoxygenation injury: with aortic clamping. XI. Cardiac advantages of normoxemic versus hyperoxemic management during cardiopulmonary bypass. *J Thorac Cardiovasc Surg* 1995;110:1255-64.
4. Morita K, Ihnken K, Buckberg GD. Studies of hypoxemic/reoxygenation injury: with aortic clamping. XII. Delay of cardiac reoxygenation damage in the presence of cyanosis: a new concept of controlled cardiac reoxygenation. *J Thorac Cardiovasc Surg* 1995;110:1265-73.
5. Ihnken K, Winkler A, Beyersdorf F, Neidhart G, Winkelmann B, Unkelbach U, et al. Reduction of oxidative damage and nitric oxid on cardiopulmonary bypass by controlling Po_2 during open heart surgery. *Circulation* 1995;92(Suppl): I763-4.
6. Ihnken K, Morita K, Buckberg GD, Sherman MP, Young HH. Studies of hypoxemic/reoxygenation injury: without aortic clamping. VI. Counteraction of oxidant damage by exogenous antioxidants: *N*-(2-mercaptopropionyl) glycine and catalase. *J Thorac Cardiovasc Surg* 1995;110:1212-20.

7. Del Nido PJ, Mickle DAG, Wilson GJ, Benson LN, Coles JG, Trusler GA, et al. Evidence of myocardial free radical injury during elective repair of tetralogy of Fallot. *Circulation* 1987; 76(Suppl):V174-9.

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Reply to the Editor:

We studied lipid peroxidation in adult patients undergoing cardiopulmonary bypass (CPB) for routine coronary artery bypass grafting (CABG). Assumptions about lipid peroxidation based on observations in immature piglets and cyanotic children with tetralogy of Fallot¹ may not be reliably transferred to adult human beings. During CPB, lipid peroxidation may well vary in different settings. Morita,² Ihnken,³ and their associates measured conjugated dienes and malondialdehyde as markers of lipid peroxidation in the myocardium of immature piglets and found a significant increase 5 minutes after the start of CPB. However, Davies and coworkers⁴ measured lipid peroxidation in the coronary sinus in adult patients undergoing routine CABG and found no significant changes during CPB. The only related study seems to be an abstract reporting the results of a comparison between hyperoxic (Po_2 400 mm Hg) and normoxic (Po_2 150 mm Hg) CPB in 20 adult patients (63 ± 8 years) undergoing CABG.⁵ Unfortunately, several questions arise from this report. Apart from being a very small study, the number of patients in each of the two groups was not stated. Crossclamp times and CPB times between the two groups were not compared, although their significance in lipid peroxidation is beyond question. Longer ischemic damage in the normoxic group might well have resulted in higher creatine kinase and malondialdehyde levels. Therefore our comment that "the contribution of hyperoxia to free radical generation and consequent lipid peroxidation in adult cardiac operations has to date not been addressed" should not be dismissed lightly.

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REFERENCES

1. Del Nido PJ, Mickle DAG, Wilson GJ, Benson LN, Coles JG, Trusler GA, et al. Evidence of myocardial free radical injury during elective repair of tetralogy of Fallot. *Circulation* 1987; 76(Suppl):V174-9.
2. Morita K, Ihnken K, Buckberg GD, Sherman MP, Young HH. Studies of hypoxemic/reoxygenation injury: without aortic clamping. IX. Importance of avoiding perioperative hyperoxemia in the setting of previous cyanosis. *J Thorac Cardiovasc Surg* 1995;110:1235-44.
3. Ihnken K, Morita K, Buckberg GD. Studies of hypoxemic/reoxygenation injury: with aortic clamping. XI. Cardiac advan-

- tages of normoxemic versus hyperoxemic management during cardiopulmonary bypass. *J Thorac Cardiovasc Surg* 1995;110:1255-64.
4. Davies SW, Underwood SM, Wickens DG, Feneck RO, Dormandy TL, Walesby RK. Systemic pattern of free radical generation during coronary bypass surgery. *Br Heart J* 1990; 64:236-40.
 5. Ihnken K, Winkler A, Beyersdorf F, Neidhart G, Winkelmann B, Unkelbach U, et al. Reduction of oxidative damage and nitric oxide on cardiopulmonary bypass by controlling PO_2 during open heart surgery (abstract). *Circulation* 1995; 92(Suppl):I763-4.

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