Cardiovascular Research, 27(11):2083-2084 (1993).

Letter to the Editor

Recovery of hypoxic neonatal hearts after cardioplegic arrest

Sir: – With regard to the article by Feldbaum *et al*[1] and Dr Baker's comments,[2] we believe that a few critical points were missed.

First, in the authors' protocol, hearts from hypoxic animals (presumed $P_aO_2 < 4.16$ kPa, 32 mm Hg) were acutely exposed to a medium containing 95% O_2 ($P_aO_2 = 89$ kPa, 686 mm Hg) at the onset of the in vitro perfusion. This may have led to significant reoxygenation injury[3–6] *before* baseline evaluation. This possibility, consistent with Dr Baker's consideration that these preparations were functionally compromised at baseline evaluation,[2] may considerably weaken the authors' conclusion that hypoxic immature rabbit hearts can recover from an ischaemic insult as well as matched controls.

Furthermore, the cited references do not support the authors' view that "cyanotic infants recover as well as non-cyanotic infants after heart surgery". For instance, Rizzoli *et al*[7] and Sunderland *et al*[8] consider cyanotic patients only, while Jonas *et al*[9] and Friedli *et al*[10] make no comparisons between cyanotic and non-cyanotic groups. Therefore, the general consensus now is that injury in cyanotic hearts is more severe than in non-cyanotic hearts.[6]

We believe that other crucial data should be made available to allow a better understanding of importance of the authors' work:

(1) Blood gases in the living animals, because the calculation of P_AO_2 from FIo_2 critically depends on ventilation, alkalosis, and acclimatisation. Assessing whether animals were adapted to hypoxia is critical because acclimatisation implies alterations of plasma (and thus intracellular) pH[11,12] and of bioenergetic patterns.[13,14]

(2) P_vO_2 and/or lactate output, to evaluate the bioenergetic pattern and to understand whether different degrees of anaerobic metabolism have protected against ischaemia/reperfusion, especially in view of the different ages of the animals and the known age related differences of myocardial metabolism.[15–17]

(3) Some evaluation of the diastolic function, as for example the pressure-volume curve, to understand postischaemic ventricular dysfunction in control and hypoxaemic/reoxygenated hearts.[18]

Finally, the Authors have reported that "some hearts no longer functioned at the postischaemic measurement time", and that they "analysed values of 0 for all variables in such hearts". Thus a quantitative variable (number of deaths) was transformed into a qualitative one (value = 0). We wonder whether statistical evaluation may have been severely compromised since n ranged from 6 to 11 in the various groups.

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1 Feldbaum DM, Kohman LJ, Veit LJ. Recovery of hypoxic neonatal hearts after cardioplegic arrest. *Cardiovasc Res* 1993;**27:** 1123–6.
2 Baker JE. Invited letter to the Editor: Recovery of hypoxic neonatal hearts after cardioplegic arrest. *Cardiovasc Res* 1993; **27:**1135–6.
3 Samaja M, Motterlini R, Santoro F, Dell'Antonio G, Corno AF. Oxidative injury in reoxygenated and reperfused hearts. *Free Rad Biol Med* (in press).
4 Corno AF, Motterlini R, Brenna L, Santoro F, Samaja M. Ischaemia/reperfusion in the posthypoxaemic re-oxygenated myocardium: haemodynamic study in the isolated perfused rat heart. *Perfusion* 1993;**8:**113–8.
5 Corno AF, Samaja M. Letter to the Editor: The reoxygenation phenomenon. *J Thorac Cardiovasc Surg* 1993;**105:**373.
6 del Nido PJ, Mickle DAG, Wilson GJ, *et al*. Evidence of myocardial free radical injury during elective repair of tetralogy of Fallot. *Circulation* 1987;**76:**174–9.
7 Rizzoli G, Mazzucco A, Fracasso A, Stellin G, Rubino M, Gallucci V. Early and late results after repair of tetralogy of Fallot. *Eur J Cardiovasc Surg* 1990;**4:**371–6.
8 Sunderland CO, Matarazzo RG, Lees MH, *et al*. Total correction of tetralogy of Fallot in infants. Postoperative hemodynamic evaluation. *Circulation* 1973;**48:**398–411.
9 Jonas RA, Krasna M, Sell JE, Castaneda AR. Myocardial failure is a rare cause of death after pediatric surgery. (Abstract) *J Am Coll Cardiol* 1991;**17:**110A.
10 Friedli B, Faidutti B, Oberhansli I, Rouge JC. Late results of surgery for congenital defects. *Helv Chir Acta* 1990;**57:** 533–43.
11 Milledge JS, Lahiri S. Respiratory control in lowlanders and Sherpa highlanders at altitude. *Respir Physiol* 1967;**2:**310–22.
12 Rahn H, Otis AB. Man's respiratory response during and after acclimatization to high altitude. *Am J Physiol* 1949;**157:** 445–62.
13 Hochachka PW, Matheson GO. Regulating ATP turnover rates over broad dynamic work ranges in skeletal muscles. *J Appl Physiol* 1992;**73:**1697–703.
14 Harris DA, Das AM. Control of mitochondrial ATP synthesis in the heart. *Biochem J* 1991;**280:**561–73.
15 Murashita T, Kempsford RD, Hearse DJ. Age-dependent changes in the tolerance of the rabbit heart to ischemia. *Eur J Cardiothorac Surg* 1990;**4:**492–8.
16 Lopaschuk GD, Spafford MA. Energy substrate utilization by isolated working hearts from newborn rabbits. *Am J Physiol* 1990; **258:**H1274–80.
17 Lopaschuk GD, Collins-Nakai RL, Itoi T. Developmental changes in energy substrate use by the heart. *Cardiovasc Res* 1992;**26:** 1172–80.
18 Corno AF, Bethencourt DM, Laks H, *et al*. Myocardial protection in the neonatal heart. *J Thorac Cardiovasc Surg* 1987;**93:** 163–72.