Author's reply

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Sir: Dr. Ipsiroglu et al. comment that cerebral blood flow velocity is influenced by numerous factors including blood gas and behavioural condition on examination. They also suggest that cerebral blood flow velocity changed dramatically in ultra-early neonatal period. Our study did not include blood gas analysis and blood pressure monitoring. The first group (0–3 h) consisted of five members, aged 1, 1.5, 2, 2, 3 h, and were examined in a non-crying state with careful handling. Therefore we cannot comment on haemodynamics in the ultra-early neonatal period. We agree with the comment of Ipsiroglu et al. that the cerebral haemodynamics in neonates is influenced by multiple factors. Not only blood gas and pressure, but also haematocrit and closure of the PDA affect cerebral blood velocity in the neonate [1, 2]. We concluded that normal values of chronological changes of cerebral blood flow velocity in the normal term neonates are necessary. For the evaluation of variable pathological conditions, values need to be compared with normals. Detailed evaluation of cerebral flow velocity during the ultra-early neonatal period before 1 h after birth is recommended.

References

1. Maertzdorf WJ, Tangelder GJ, Slaaf DW, Blanco CE (1989) Effects of partial plasma exchange transfusion on cerebral blood flow velocity in polycythaemia preterm, term and small for date newborn infants. Eur J Pediatr 148:774–778
2. Wright LL, Baker KR, Hollander D, Wright JN, Nagey DA (1988) Cerebral blood flow velocity in term newborn infants: changes associated with ductal flow. J Pediatr 112:463–773

Uridine preserves the expression of respiratory enzyme deficiencies in cultured fibroblasts

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Sir: The expression of respiratory enzyme deficiencies in cultured cells in uncertain and frequently transient [1, 4]. This could result either from the failure of respiratory-enzyme-deficient cells to grow normally or from the re-expression of fetal and embryonic isozymes in cultured cells. Whatever the mechanism, this feature hampers prenatal diagnosis of these conditions using chorionic villi or amniotic fluid cells in at-risk families.

It has been recently shown that cells lacking respiratory enzymes require an exogenous supply of uridine for normal growth due to the functional impairment of the respiratory chain-dependent dihydroorotate dehydrogenase [2, 3]. For this reason, we hypothesised that adding uridine, whose production depends on the dihydroorotate dehydrogenase reaction, to the culture medium might help to maintain expression of respiratory enzyme deficiencies in cultured cells.

We found that, in the absence of uridine, the cytochrome c oxidase/succinate cytochrome c reductase (COX/SCCR) activity ratios of COX-deficient strains gradually increased and reached normal values as the cell culture proceeded (Fig. 1). On the other hand, in the presence of uridine (200 μM), the enzyme activity ratios of the deficient cell lines remained very low regardless of the number of cell population doublings. However, uridine did not alter the enzyme activity ratios in the control cell line (Fig. 1).

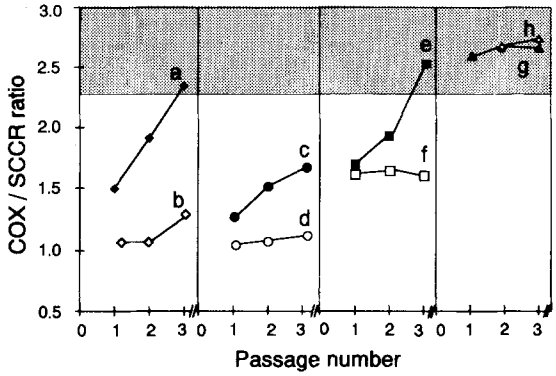

Fig. 1. Effect of uridine on cytochrome c oxidase deficiencies in cultured fibroblasts. Ratios of cytochrome c oxidase (COX) to succinate cytochrome c reductase (SCCR) activities were measured in the absence *(a, c, e, g)* or in the presence *(b, d, f, h)* of uridine. Values are the mean of three different measurements. Fibroblasts from patient *(a–f)* and control *(g, h)* were cultured in RPMI 1640 medium (GIBCO) supplemented with 10% SVF, 2 m*M* glutamine, 2.5 m*M* Na-pyruvate and with or without 200 μ*M* uridine

The present results demonstrate that culture medium supplemented with uridine maintains the expression of respiratory enzyme deficiencies in cultured fibroblasts, provided it is added early.

While genetic counselling for respiratory enzyme deficiencies has long been difficult due to the uncertain expression of the disease in cultured amniocytes, the present findings will hopefully contribute to the early and reliable prenatal diagnosis of these conditions.

References

1. Bourgeron T, Chretien D, Rötig A, Munnich A, Rustin P (1992) Prenatal diagnosis of cytochrome c oxidase deficiency in cultured amniocytes is hazardous. Prenat Diagn 12:548–549
2. King MP, Attardi G (1989) Human cells lacking mtDNA: repopulation with exogenous mitochondria by complementation. Science 246:500–503
3. Morais R, Grégoire M, Jeannotte L, Gravel D (1990) Chick embryo cells rendered respiration-deficient by chloramphenicol and ethidium bromide are auxotrophic for pyrimidines. Biochem Biophys Res Commun 94:71–77
4. Robinson BH, Glerum DM, Chow W, Petrova-Benedict R, Lightowlers R, Capaldi R (1990) The use of skin fibroblast cultures in the detection of respiratory chain defect in patients with lacticacidemia. Pediatr Res 28:549–555