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Letter to the Editor: Measurement of Pyruvate Carboxylase Activity in Amniotic Fluid Cells

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In a recent article, Atkin *et al.* (1) reported a patient with deficient pyruvate carboxylase (PC) activity in cultured skin fibroblasts and peripheral blood leukocytes as well as in the liver. Because PC deficiency is manifested clinically by developmental delay and ultimately death and because most attempts at treatment have been unsuccessful (4), the need for prenatal diagnosis is obvious. Although the potential for prenatal diagnosis of PC deficiency using cultured amniotic fluid cells was suggested by Atkin *et al.* (1), to our knowledge there has been no documentation of measurable activity in this tissue source. However, we have recently measured PC activity in cultured amniotic fluid cells and have found enzyme activity comparable to that in cultured skin fibroblasts.

PC activity of skin fibroblasts and amniotic fluid cells was measured by the procedure of Wolf *et al.* (5) with the following modifications: the cell extracts were prepared with 0.05% Triton X-100 (Sigma Chemical Co.), and 0.175 mM acetyl CoA (Sigma Chemical Co.) and 3 mM sodium pyruvate were added in place of propionyl CoA. PC activity in fibroblast culture extracts derived from seven unaffected individuals was 529 ± 212 pmol/min/mg protein (mean ± SD) with a range of 260 to 940 pmol/min/mg at 37°; the enzyme activity from three patients with PC deficiency (1–3) was confirmed to be less than 3% of normal (12–13 pmol/min/mg protein). The PC activity in 14 amniotic fluid cell extracts (30–90 μg protein) was 461 ± 222 pmol/min/mg with a range of 127 to 766 pmol/min/mg. Amniocentesis was performed in all individuals because of advanced maternal age. Gestational ages were between 14 and 20 weeks. The cell cultures were studied at confluence or near-confluence between one and four passages.

We recommend that patients suspected of having an error in pyruvate metabolism and with clinical features suggestive of PC deficiency be studied for enzyme activity in their peripheral blood leukocytes or skin fibroblasts. Then, if the patient is shown to have PC deficiency, the mother's future pregnancies should be monitored by amniocentesis and assay of PC activity in amniotic fluid cells. Although we have not had the opportunity to diagnose an affected fetus, our demonstration that PC activity is detectable in cultured amniotic fluid cells adds yet another inborn error of metabolism to the growing list of disorders that can potentially be diagnosed prenatally.

REFERENCES AND NOTES

1. Atkin, B. M., Utter, M. F., and Weinberg, M. B.: Pyruvate carboxylase and phosphoenulpyruvate carboxykinase in leukocytes and fibroblasts from a patient with pyruvate carboxylase deficiency. Pediatr. Res., *13:* 38 (1979).
2. Cowan, M. J., Packman, S., Wara, D. W., Ammann, A. J., Yoshino, M., Sweetman, L., and Nyhan, W.: Multiple biotin-dependent carboxylase deficiencies associated with defects in T-cell and B-cell immunity. Lancet, *2:* 115 (1979).
3. DeVivo, D. C., Haywood, M. W., Leckie, M. P., Bussman, Y. L., McDougal, D. B., and Pagliara, A. S.: The clinical and biochemical implications of pyruvate carboxylase deficiency. J. Clin. Endocrinol. Metab., *45:* 1281 (1977).
4. Tanaka, K., and Rosenberg, L. E.: Metabolism of amino acids and organic acids. In: N. Freinkel: Contemporary Metabolism. Vol. 1, p. 461 (Plenum Medical Press, New York, 1979).
5. Wolf, B., Hsia, Y. E., and Rosenberg, L. E.: Biochemical differences between mutant propionyl-CoA carboxylases from two complementation groups. Am. J. Hum. Genet., *30:* 455 (1978)
6. Requests for reprints should be addressed to: Dr. Barry Wolf, Department of Human Genetics, Medical College of Virginia, P.O. Box 33, MCV Station, Richmond, VA 23298 (USA).

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