Letter to the Editor: White Cell Ornithine Transcarbamylase Activity Cannot Detect the Liver Enzyme Deficiency

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We have been unable to confirm the report of Wolfe and Gatfield (3) that assay of ornithine transcarbamylase (OTC) in leukocytes can substitute for assay of this enzyme in a liver biopsy in order to make a diagnosis of ornithine transcarbamylase deficiency.

Leukocytes were prepared from 40 ml blood as follows: red cells were settled in Plasmagel (HTI Corp., Buffalo, NY), the plasma and white cells aspirated and the white cells centrifuged to form a pellet. The white cells were washed first with isotonic NaCl, then for 45 sec in distilled water to lyse red cells, and finally three times in 0.05 M NaCl. The centrifuged leukocyte pellet was frozen at

1 shows that urea cycle enzyme activities in the liver homogenates were within or close to the normal range except for OTC, which was 10%, 6%, and 13%, respectively, of the appropriate normal mean values (3). The white cell OTC activities bore no relationship to the liver deficiencies, being 1500%, 98% and 1700% of the control mean value. One patient (S.B.) also had elevated values for carbamyl phosphate synthetase and argininosuccinate lyase, while one (A.H.) had low values for argininosuccinate synthetase and lyase.

These results lead us to conclude that ornithine transcarbamylase deficiency in liver cannot be inferred from the results of this

Table 1. Urea cycle enzymes^a

Tissue and Patient	Protein (mg/g) ^b	Units/mg protein ^b				
		CPS	OTC	AS	AL	Ase
Liver, needle biopsy						
A.H.	149	0.81	3.63	0.36	0.89	295
Controls, mean ³	169	1.63	34.6	0.33	1.00	274
Controls, SD	20	0.42	4.2	0.10	0.18	64
Liver, wedge biopsy						
A.W.	90	2.44	2.72	0.57	1.83	569
S.B.	122	1.24	5.91	0.26	1.28	431
Controls, mean ³	145	1.91	44.2	0.62	1.49	579
Controls, SD	20	0.27	7.7	0.14	0.26	106
Protein (mg/ml) ^b						
Leukocytes, frozen						
A.H.	5.88	0.009	0.971	0.054	0.068	11.9
A.W.	2.88	0.008	0.062	0.486	0.326	10.2
S.B.	1.37	0.097	1.080	0.278	0.759	25.1
Controls (14), mean	6.50	0.003	0.063	0.331	0.232	22.5
Controls, SD	1.31	0.003	0.093	0.118	0.076	12.2
Controls, range, min		0.000	0.002	0.181	0.154	7.6
Controls, range, max		0.009	0.345	0.535	0.398	46.7

^a CPA: carbamyl phosphate synthetase; OTC: ornithine transcarbamylase; AS: argininosuccinic acid synthetase; AL: argininosuccinic acid lyase; Ase: arginase.

^b One unit equals 1 μ mol product formed/hr; liver protein is milligrams per g wet wt; leukocyte protein is milligrams per ml of cell homogenate.

–60° for less than 3 days, thawed, 1.4 ml of distilled water added, frozen and thawed three times and the cell suspension was homogenized with a Polytron tissue homogenizer for 15 sec. The urea cycle enzymes were assayed under conditions optimal for the human enzymes (1). OTC and carbamyl phosphate synthetase assays contained 0.1 ml of undiluted homogenate in the 0.3 ml assay mixture and were incubated for 1 hr at 37°. Table 1 shows the normal values obtained on 14 healthy adults. No differences were noted between fresh or frozen white cell pellets. The range of normal values is very wide for OTC, and carbamyl phosphate synthetase activity is almost undetectable.

Three female patients with the typical clinical syndrome of OTC deficiency and with hyperammonemia during febrile illnesses or unrestricted ingestion of protein underwent biopsies of the liver, which were frozen at –60° and assayed within 3 days. White cells were prepared as above and assayed in 3 days. Table

enzyme's activity in peripheral leukocytes, but that liver biopsy is still necessary to confirm the diagnosis. Further correlations are necessary to conclude that liver deficiencies of the other enzymes can be detected in leukocytes.

REFERENCES

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3. Wolfe, D. M., and Gatfield, P. D.: Leukocyte urea cycle enzymes in hyperammonemia. *Pediat. Res.*, 9: 531 (1975).

Note: A rebuttal to this letter will be forthcoming from D. M. Wolfe.