References and Notes

1. C. M. Armstrong, *Q. Rev. Biophys.* **7**, 179 (1975).
2. _____, F. Bezanilla, E. Rojas, *J. Gen. Physiol.* **62**, 375 (1973).
3. C. Sevcik and T. Narahashi, *J. Membr. Biol.* **24**, 329 (1975).
4. E. Rojas and B. Rudy, *J. Physiol. (London)* **262**, 501 (1976).
5. C. M. Armstrong and F. Bezanilla, *J. Gen. Physiol.* **70**, 567 (1977).
6. D. C. Eaton, M. S. Brodwick, G. S. Oxford, B. Rudy, *Nature (London)* **271**, 473 (1978).
7. *Calbiochem Catalog* (Calbiochem, La Jolla, Calif., 1978), p. 163.
8. H. M. Fishman, *Biophysical Journal* **10**, 799 (1970).
9. C. Tanford and J. D. Hauenstein, *J. Am. Chem. Soc.* **78**, 5287 (1956).
10. S. Terakawa and A. Watanabe, *Jpn. J. Physiol.* **26**, 693 (1976).
11. G. E. Means and R. E. Feeney, *Chemical Modification of Proteins* (Holden-Day, San Francisco, 1971).
12. D. R. Phillips and M. B. Morrison, *Biochemistry* **10**, 1766 (1971).
13. G. Oxford, C. Wu, T. Narahashi, *J. Gen. Physiol.* **71**, 227 (1978).
14. Y. Nazaki and C. Tanford, *J. Biol. Chem.* **246**, 2211 (1971).
15. J. P. Riehm *et al.*, *Biochemistry* **4**, 760 (1965).

16. This work was supported by NIH grant NS-11963.

19 December 1977; revised 27 February 1978

Cystic Fibrosis: Decreased Conjugation and Excretion of [^{14}C]Spermidine

Abstract. *Free and conjugated [^{14}C]spermidine were measured in plasma samples from normal individuals and cystic fibrosis patients. Within 4 minutes, the ^{14}C-labeled material in the plasma from normal individuals was 70 percent conjugated compared to no detectable conjugation by cystic fibrosis patients. Further, the patients excreted only 11 to 13 percent of the [^{14}C]spermidine in their urine within 72 hours whereas normal excretion was 60 to 76 percent. In both cases, the labeled material was in a conjugated form.*

Cystic fibrosis is an autosomal recessive genetic disorder characterized by pancreatic dysfunction and obstructive pulmonary disease (*1, 2*). The increased and abnormally viscous secretions of mucus that also characterize the disease may be a result of abnormalities in all exocrine glands (*2*). Although there have been several attempts to characterize this disease on a biochemical basis, the underlying metabolic defect remains obscure (*3*).

Several studies have shown that polyamine levels in whole blood are altered in cystic fibrosis patients (*4, 5*). Cohen *et al.* (*5*) found that concentrations of spermidine in erythrocytes were elevated to 150 percent as compared to those of controls, and that the spermine content in lymphocytes and granulocytes was decreased. Although Rosenblum *et al.* reported that all three polyamines (putrescine, spermidine, and spermine) were elevated 2- to 30-fold in the urines of patients with cystic fibrosis, patients who had been given a tracer dose of [^{14}C]spermidine excreted only 11 to 13 percent of the labeled material in their urines within 72 hours compared to 60 to 76 percent excreted by normal individuals in the same period (*6*). In this study we report that cystic fibrosis patients do not exhibit the rapid conjugation of [^{14}C]spermidine observed in normal individuals and patients with cancer (Fig. 1), conjugation that appears necessary for its excretion (*7*). These data support the proposition that polyamine metabolism is altered in, and related to, the pathology of cystic fibrosis.

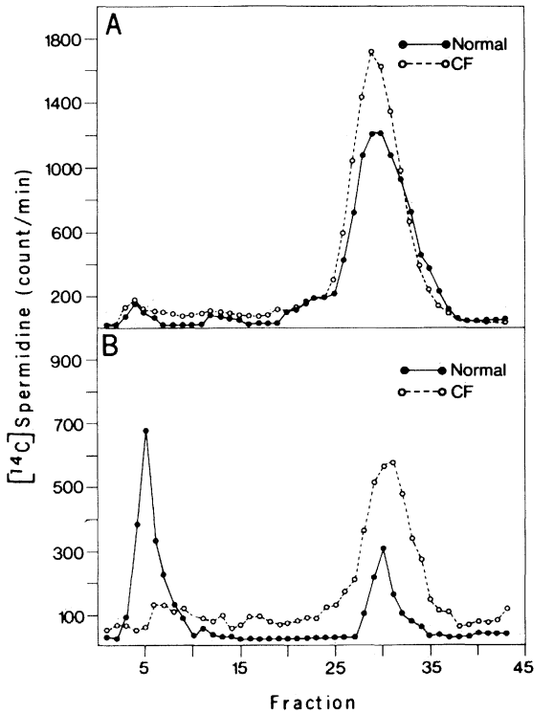

Fig 1. Dowex chromatography of plasma from normal and cystic fibrosis (*CF*) patients (A) 1 minute and (B) 4 minutes after intravenous [^{14}C]spermidine injection. The radiolabeled material was eluted with 2*M* to 5*M* linear NaCl gradient and collected in 1-ml fractions. Free [^{14}C]spermidine eluted in fractions 25 to 35, whereas conjugated [^{14}C]spermidine eluted in fractions 3 to 9.

Venous blood samples were taken at 1-minute intervals for 10 minutes after injection of [^{14}C]spermidine (100 μCi, 12.5 mCi/mmole). Total urine output was collected for 3 days after the injection. To separate free from conjugated [^{14}C]spermidine, samples of plasma or urine were chromatographed on Dowex 50W × 8 with a linear NaCl gradient (*8*). Chromatography of plasma samples from normal individuals (two male, two female, mean age 25 years) showed that, after 4 minutes, 70 percent of the [^{14}C]spermidine had been conjugated (Fig. 1). Cystic fibrosis patients (one male, one female, mean age 27 years, NIH clinical score <50) failed to demonstrate any conjugation after 4 minutes. Analysis of the labeled material in the urine showed that both normals and cystic fibrosis patients excreted more than 90 percent of the [^{14}C]spermidine in a conjugated form (data not shown). This suggests that conjugation, although delayed, does take place in cystic fibrosis patients. Sephadex G-25 chromatography of the polyamine conjugate isolated from normal individuals and cancer patients suggests that it has a molecular weight of 1000 (*9*).

On the basis of their studies of hepatectomized rats, Rosenblum and Russell (*8*) suggested that polyamine conjugation might occur in the liver. Although the occurrence of hepatic cirrhosis in cystic fibrosis has been well documented, the two patients we studied showed no clinical evidence of hepatic dysfunction. However, both cyctic fibrosis patients in this study received trimethoprim (Bactrim, Roche) therapy, and we cannot rule out the possibility that the delayed conjugation may be a drug effect, even though cancer patients receiving trimethoprim therapy did not have altered polyamine conjugation patterns.

It is not known whether delayed conjugation and sequestration of [^{14}C]spermidine represents a primary genetic expression of the disease or a secondary ef-

0036-8075/78/0630-1496$00.50/0

fect produced by the pathological consequences of the disease. It is possible that elevated spermidine in red blood cells of patients with cystic fibrosis is related to a conjugation defect that inhibits excretion, since the addition of exogenous spermidine to membranes alters their properties (*10*). A decreased spermidine excretion and consequent extracellular increase, therefore, could contribute to the membrane pathology associated with cystic fibrosis.

MICHAEL G. ROSENBLUM
BRIAN G. M. DURIE
ROBERT C. BECKERMAN
LYNN M. TAUSSIG
DIANE HADDOCK RUSSELL
Department of Pharmacology,
University of Arizona
Health Sciences Center, Tucson 85724

References and Notes

1. D. H. Andersen, *Am. J. Dis. Child.* **56**, 344 (1976); P. A. diSant'Agnese and R. C. Talamo, *N. Engl. J. Med.* **277**, 1287, 1355, 1399 (1967).
2. P. A. diSant'Agnese, R. C. Darling, G. A. Perera, E. Shea, *Pediatrics* **12**, 549 (1953).
3. L. M. Taussig and L. I. Landau, in *Kelly's Practice of Pediatrics*, V. Kelly, Ed. (Harper & Row, Hagerstown, Md., 1976), vol. 4, p. 1; B. Bowman, L. Lockhart, M. McCombs, *Science* **164**, 325 (1969).
4. D. Lundgren, P. Farrell, P. diSant'Agnese, *Clin. Chim. Acta* **62**, 357 (1975).
5. L. F. Cohen, D. W. Lundgren, P. M. Farrell, *Blood* **48**, 469 (1976).
6. M. G. Rosenblum *et al.*, *Pediatr. Res.*, in press.
7. D. H. Russell, *Clin. Chem (Winston-Salem, N.C.)* **23**, 22 (1977).
8. M. G. Rosenblum and D. H. Russell, *Cancer Res.* **37**, 47 (1977).
9. M. G. Rosenblum *et al.*, *Proc. Am. Assoc. Cancer Res.* **17**, 15 (1976).
10. N. Seiler and K. Deckart, *Neurochem. Res.* **1**, 469 (1976).
11. Supported by PHS grants CA-14783 and CA-00072 (to D.H.R.). B.G.M.D. is a scholar of the Leukemia Society of America and R.C.B. is a clinical fellow of the American Lung Assoc.

24 February 1978

Is Binocular Vision Always Monocular?

Abstract. *Visual sensitivity of one eye was determined under binocular stimulus conditions yielding apparent fusion, stereopsis, monocular dominance, and monocular suppression. Marked losses in sensitivity accompanied monocular suppression but were not evident during stable single vision. The results are inconsistent with the hypothesis that suppression alone mediates binocular single vision.*

The singleness of binocular vision is so immediate and compelling that we are seldom aware of its dual monocular origins. Evidently inputs from the two eyes are unified by the brain, but the details of this inconspicuous process are incomplete. The most popular theory of binocular single vision assumes that the two monocular inputs are combined, or fused, in a cooperative fashion, such that each eye contributes more or less equally to the final binocular product (*1*). There is, however, an alternative theory that assumes that we actually see with only one eye at a time, owing to suppression of the partner eye's information (*2, 3*). This so-called suppression theory, although somewhat counterintuitive, accounts for a variety of perceptual outcomes that are troublesome for fusion theory (*3*), and it is not incompatible with the occurrence of stereoscopic depth perception (*4*).

Because the two eyes ordinarily share a common view, phenomenal observation cannot tell us which process, fusion or suppression, operates to promote single vision (*5-7*). Suppression is evident, however, when the two eyes receive different views by dichoptic stimulation; instead of stable single vision, this situation produces alternating periods of dominance and suppression between the two eyes, an outcome known as binocular rivalry. Indeed, this phenomenon of binocular rivalry has served as a major impetus for suppression theories of binocular single vision. Work on binocular rivalry has shown that phenomenal suppression is accompanied by a general decrease in the visual sensitivity of the suppressed eye, relative to the eye's sensitivity during dominance (*8*). Now, if binocular vision always involves suppression, even under normal viewing conditions, losses in visual sensitivity should be a symptom of suppression when the two eyes receive identical stimulation. We have tested this possibility by measuring monocular detection thresholds under stimulus conditions yielding stereopsis, apparent fusion, monocular dominance, and monocular suppression.

Observers with excellent acuity and stereopsis viewed displays generated electronically on two cathode-ray tube (CRT) displays and presented separately to the two eyes by a mirror stereoscope. Each display consisted of a rectangular field, 8° by 10° of visual angle, produced by placing a translucent mask over the CRT screen; the luminance of this surround field was 1.7 cd/m^2. In the center of each field was a circular aperture, 1° of visual angle in diameter, through which the CRT screen was exposed. Within each circular area could be displayed sinusoidal grating patterns, either vertical or horizontal, or a homogeneous area of the same average luminance as the grating, 5.1 cd/m^2. A briefly flashed spot of light 10 minutes in diameter could be superimposed optically in either the upper or lower portion of the circular target viewed by the left eye. Observers triggered the flash by depressing a button and indicated with a lever switch whether the flash appeared in the upper or lower position (*9*).

We began by determining for each observer the flash duration yielding approximately 90 percent correct performance when the left eye, which received the test flash, was dominant; durations ranged from 9.5 to 12 msec among observers. To promote dominance a 6 cycle/deg vertical grating was presented to the left eye while the right eye viewed a homogeneous field; grating contrast was 1 log unit above threshold, a value that ensured continuous visibility of the pattern (condition MD); these values

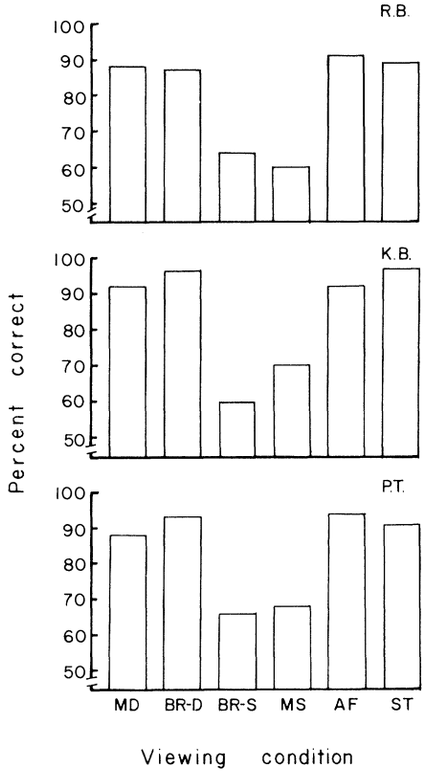

Fig. 1. Correct detection for each observer on a two-alternative forced-choice task. A small, brief test flash was presented in either the upper or lower portion of the display viewed by the left eye. The flash was delivered while the left eye was continuously dominant (*MD*), intermittently dominant (*BR-D*), intermittently suppressed (*BR-S*), continuously suppressed (*MS*), or while the left and right eye patterns were apparently fused (*AF*) and generated a stereoscopic sensation of depth (*ST*). Performance for conditions *BR-S* and *MS* differed significantly ($P < .01$) from all other conditions. Each value is based on at least 100 trials.

0036-8075/78/0630-1497$00.50/0