by Dr. R. Matalon (*20*) and found to be normal in the livers of S.H. and control subjects.

With the possible exception of Fabry's disease and the adult form of Gaucher's disease (*4*), which both spare the nervous system, all the glycosphingolipidoses so far described are characterized by an almost total specific enzyme deficiency and rapid neurological deterioration after the first few months of life. In contrast to this, S.H. appeared to develop normally, although somewhat slowly, for 2½ years before the start of progressive neurologic degeneration. Because of the central role of GL-2 in both major glycosphingolipid catabolic pathways, a total enzyme deficiency should be at least as severe as infantile Gaucher's disease; the finding of partial lactosyl ceramidase activity in our patient can be interpreted as an explanation for the more prolonged course of the disease. The discovery of this disorder means that an enzyme defect is known for each step in the catabolism of red cell globoside to ceramide. Further, four clinically distinct glycosphingolipidoses, namely, generalized gangliosidosis, Fabry's disease, Krabbe's leukodystrophy (*21*), and lactosyl ceramidosis have now been attributed to specific galactosyl hydrolase deficiencies. Even though these four enzymes have not been characterized, nevertheless the use of specific substrates enables us to detect the diseases and to offer genetic counseling.

GLYN DAWSON
ARTHUR O. STEIN
*Departments of Pediatrics* and *Biochemistry, Joseph P. Kennedy, Jr., Mental Retardation Research Center, University of Chicago, Chicago, Illinois 60637*

### References and Notes

1. K. Sandhoff, *Fed. Eur. Biochem. Soc. Lett.* **4**, 351 (1969).
2. K. Sandhoff, U. Andreae, H. Jatzkewitz, *Life Sci.* **7**, 283 (1968).
3. C. C. Sweeley and B. Klionsky, in *The Metabolic Basis of Inherited Disease*, J. B. Stanbury, J. B. Wyngaarden, D. S. Fredrickson, Eds. (McGraw-Hill, New York, 1966), p. 618; R. O. Brady, A. E. Gal, R. M. Bradley, E. Martenson, A. L. Warshaw, L. Laster, *N. Engl. J. Med.* **276**, 1163 (1967); C. A. Mapes, R. L. Anderson, C. C. Sweeley, *Fed. Eur. Biochem. Soc. Lett.* **7**, 180 (1970).
4. R. O. Brady, J. N. Kanfer, D. Shapiro, *Biochem. Biophys. Res. Commun.* **18**, 221 (1965).
5. J. S. O'Brien, M. B. Stern, B. H. Landing, J. K. O'Brien, A. Donnel, *Amer. J. Dis. Child.* **109**, 338 (1965); S. Okada and J. S. O'Brien, *Science* **160**, 1002 (1968).
6. L. Svennerholm, *Biochem. Biophys. Res. Commun.* **9**, 436 (1962); S. Okada and J. S. O'Brien, *Science* **165**, 698 (1969); E. H. Kolodny, R. O. Brady, B. W. Volk, *Biochem. Biophys. Res. Commun.* **37**, 526 (1969); B. Hultberg, *Lancet* **1969-II**, 1195 (1969).
7. Abbreviations: cer, ceramide or 2-*N*-acylsphingosine; galNAc, *N*-acetylgalactosamine; gal, galactose; glc, glucose; NANA, *N*-acetylneuraminic acid; $SO_3H$, sulfate. GL-1, GL 2, GL-3, and GL-4 are explained in Fig. 1.
8. J. Folch, M. Lees, G. H. Sloane-Stanley, *J. Biol. Chem.* **226**, 497 (1957).
9. G. Rouser, G. Kritchevsky, C. Galli, A. Yamamoto, A. G. Knudson, Jr., in *Inborn Disorders of Sphingolipid Metabolism*, S. M. Aronson and B. W. Volk, Eds. (Pergamon Press, London, 1967), p. 303.
10. D. E. Vance and C. C. Sweeley, *J. Lipid Res.* **8**, 621 (1967).
11. R. Matalon, A. Dorfman, G. Dawson, C. C. Sweeley, *Science* **164**, 1522 (1969).
12. J. R. Wherrett, *Neurology* **19**, 489 (1969).
13. Normal liver contains 0.17 μmole per gram of $G_{M3}$ (fresh weight), representing approximately 50 percent of the total glycosphingolipid content.
14. R. J. Desnick, personal communication. In the urine sediments of patients there is a tenfold excess of GL-1 in Gaucher's, GL-3 in Fabry's, and GL-4 in Sandhoff's (visceral Tay-Sachs) diseases.
15. G. Dawson, R. Matalon, A. O. Stein, in preparation.
16. J. Menkes, C. Duncan, J. Moossy, *Neurology* **16**, 581 (1966); J. E. Evans and R. H. McCluer, *J. Neurochem.* **16**, 1393 (1969).
17. K. Suzuki and G. C. Chen, *J. Lipid Res.* **8**, 105 (1967); H. Pilz, K. Sandhoff, H. Jatzkewitz, *J. Neurochem.* **13**, 1273 (1966).
18. M. Philippart, B. Rosenstein, J. H. Menkes, *J. Neuropathol. Exp. Neurol.* **24**, 290 (1965).
19. This compound was a gift from Dr. N. Radin, Mental Health Research Institute, University of Michigan, Ann Arbor. See N. S. Radin, L. Hof, R. M. Bradley, R. O. Brady, *Brain Res.* **14**, 497 (1969).
20. We thank Dr. R. Matalon, Department of Pediatrics, University of Chicago, for help and advice with the enzyme studies.
21. M. J. Malone, *Trans. Amer. Soc. Neurochem.* **1**, 56 (1970); K. Suzuki and Y. Suzuki, *Proc. Nat. Acad. Sci. U.S.* **66**, 302 (1970).
22. Supported by PHS Mental Retardation Research Center grant HD 04583-01 and USPHS grant RR 00305. We thank J. Oh for technical assistance. G.D. and A.O.S. are Joseph P. Kennedy, Jr., scholars.

4 May 1970; revised 9 July 1970

## Sodium Cyclamate and Bladder Carcinoma

It was informative to read that Bryan and Ertürk (*1*) in their first paragraph summarily discarded previous evidence of the carcinogenic effect of sodium cyclamate, notwithstanding all the pros and cons on this subject. While their data are quantitatively impressive in showing that surgically implanted pellets of cholesterol plus cyclamate result in bladder carcinomas in laboratory mice, the control category in their experiments seems to be incomplete. The central technical question at stake is which of the large variety of molecular species ingested via normal diets, when pelletized with cholesterol and implanted in this way, would give the same low incidence of carcinomas as cholesterol pellets alone.

If we ignore, as the authors did, the entire problem of which molecules would normally end up in urinary bladders in amounts similar to the cyclamate concentrations introduced by their technique, then it is interesting to speculate that sucrose, for example, might also have a carcinogenic effect under the same experimental conditions. If such a finding were documented to the same degree as in Bryan and Ertürk's report, could we legitimately conclude that sugar causes bladder carcinoma?

It seems also worth noting that the authors did not rule out the possibility of synergistic effects in their experiment.

LINCOLN PIERSON BROWER
*Department of Biology, Amherst College, Amherst, Massachusetts 01002*

### Reference

1. G. T. Bryan and E. Ertürk, *Science* **167**, 996 (1970).

23 July 1970

## LSD: Teratogenicity in Mice

Roux, Dupuis, and Aubry (*1*) report that LSD failed to cause abnormalities in rats, mice, and hamsters. I wish to comment specifically about the work performed with mouse embryos.

The teratogenic effect of injected LSD was originally demonstrated in studies on a large series of animals from several inbred mouse lines (*2*). These studies were confirmed and extended in other laboratories (*3, 4*). Dipaolo *et al.* (*4*), moreover, emphasized the fact that in their study teratogenicity was observed in inbred animals but not in outcrossed, general purpose mice. In those studies, as well as in our own, the injection of LSD appears to lead to an increased incidence of those developmental defects which also occur "spontaneously" in these lines.

There is thus no inconsistency in the reported observations. Teratogens always act against a background of genetically influenced susceptibility; LSD is no exception. But since, as the authors point out, extrapolation to man is difficult and extensive clinical observations are needed, one must in the interim at least recognize that LSD can be teratogenic in mice.

ROBERT AUERBACH
*Department of Zoology, University of Wisconsin, Madison 53706*

### References

1. C. Roux, R. Dupuis, M. Aubry, *Science* **169**, 588 (1970).
2. R. Auerbach and J. A. Rugowski, *ibid.* **157**, 1325 (1967).
3. J. K. Hanaway, *ibid.* **164**, 574 (1969).
4. J. A. Dipaolo, H. M. Givelber, H. Erwin, *Nature* **220**, 490 (1968).

15 September 1970

## Sodium Cyclamate and Bladder Carcinoma

Lincoln Pierson Brower

*Science* **170** (3957), 558.
DOI: 10.1126/science.170.3957.558