Increased Susceptibility of Riboflavin Deficient Rats to Galactose Cataract

Recent studies have shown that the glutathione reductase activity of human red blood cells is strongly dependent upon the state of riboflavin nutrition[1-3]. The metabolism of the lens of the eye closely resembles red cell metabolism[4]. Because of the critical role that glutathione reduction appears to play in the defense of lens protein against precipitation as cataracts[5,6], we have investigated the role of riboflavin intake on lens glutathione reductase activity and on galactose-induced cataract.

When 23-day-old albino rats were placed on riboflavin-deficient diet (Nutritional Biochemicals Corp. USA), the average glutathione reductase activity of red cells was found to be 40% of that of a normal control group which received an identical diet, supplemented, however, with 33 mg of riboflavin/kg. The glutathione reductase activity of the lens of the rats fed the riboflavin-deficient diet for 21 days was about 75% that of the enzyme activity in the lens of rats fed the riboflavin-fortified diet. 20 rats which had been on a riboflavin-deficient diet for 21 days were placed on a 68% galactose diet (Nutritional Biochemicals Corp. USA) deficient in riboflavin. 20 rats which had been receiving the riboflavin-supplemented diet received 68% galactose diet containing 33 mg riboflavin/kg diet. They were examined ophthalmoscopically every few days. At appropriate intervals equal numbers of riboflavin-deficient and control rats were sacrificed, the degree of cataract formation in the lenses was evaluated visually, and the amount of soluble lens protein, glutathione, glutathione reductase activity and total thiol was determined. The Table shows the results of these studies.

Fifteen days after the feeding of the high-galactose diet deficient in riboflavin had been started, about 60% of rats developed mature cataracts and the remaining had severe opacity; the lenses of control rats, receiving a high-galactose diet supplemented with riboflavin, showed only slight vacuolization. 3 days later about 90% of the riboflavin-deficient rats had developed mature cataracts, whereas 80% of the control rats fed on high-galactose diet fortified with riboflavin, developed only partial subscapular cataracts. However, 26 days after feeding of the high galactose diet with riboflavin had been initiated, about 85% of control rats had also developed mature cataracts.

It is clear that riboflavin deficiency produces not only decreased lens glutathione reductase activity, but also increases susceptibility to cataract formation. Although it is attractive to suppose that mechanism of the enhanced susceptibility of these animals to cataract formation is diminished capacity to reduce glutathione, other more remote effects of riboflavin deficiency must also be considered. For example, the body weight of riboflavin-deficient animals averages 25% less than that of control animals. Further studies to delineate the role of riboflavin nutrition on susceptibility to cataract formation are clearly indicated, and may prove to be of ultimate clinical importance[7].

Protein, total thiol and glutathione reductase activity in the lens of rats kept on high galactose diet[a]

Days after feeding high galactose diet	No. of rats	Riboflavin	Protein Total mg/100 mg wet wt.	Soluble mg/100 mg wet wt.	Total thiol μmoles/100 mg wet wt.	Glutathione reductase Units/100 mg wet wt. No FAD	With FAD
0	2	+	30.0	ND[b]	2.38	12.6	18.9
	2	—	24.8	ND	2.08	9.2	13.1
8	1	+	ND[b]	36.8	ND	24.9	ND
	1	—	ND	40.0	ND	19.0	ND
20	3	+	28.0	25.6	2.53	18.6	19.9
	3	—	22.0	13.6	1.14	10.4	13.5
26	2	+	15.6	8.2	0.93	7.6	8.7
	2	—	19.6	4.8	0.43	9.0	10.3

All values are given as mean of the number of rats given in the table. [a] Conditions of experiments are described in the text. The methods of analysis have been described previously[3,6]. [b] Not done.

1 D. GLATZLE, F. WEBER and O. WISS, Experientia *24*, 1122 (1968).
2 E. BEUTLER, Science *165*, 613 (1969).
3 E. BEUTLER, J. Clin. Invest. *48*, 1957 (1969).
4 J. H. JANDL, Ann. Int. Med. *58*, 702 (1964).
5 J. H. KINOSHITA, Archives Ophthal. *72*, 554 (1964).
6 S. K. SRIVASTAVA and E. BEUTLER, Biochem. J. *112*, 421 (1969).

7 This investigation was supported in part by Public Health Service Grant No. HE 07449 from the National Heart Institute, and in part by Public Health Service Grant No. HD 01974 from the National Institute of Child Health and Human Development.

8 Chairman, Division of Medicine, City of Hope Medical Center; Clinical Professor of Medicine, University of Southern California, Los Angeles.

Zusammenfassung. Bei riboflavinarm ernährten Albinoratten beträgt die Aktivität der Erythrocyten-Glutathionreduktase nur 40% und diejenige der Augenlinsen-Glutathionreduktase 75% der Aktivität normaler Kontrolltiere und es kommt zu vorzeitigem Auftreten von Katarakten.

S. K. SRIVASTAVA and E. BEUTLER[8]

Division of Medicine,
City of Hope Medical Center,
Duarte (California 91010, USA), 20 November 1969.