Nutritional Evaluation of Flour Enrichment with Riboflavin in Israel

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In 1945 Braun, Bromberg and Brzezinski[1] reported that 190 (21 per cent) of 900 pregnant women belonging to the lower social brackets of the Jewish population of Jerusalem showed definite signs of ariboflavinosis. All patients manifested glossitis in various morphologic forms. Papillitis was observed in 70 per cent, atrophic glossitis in 25 per cent and ulcerative changes of the tongue with desquamation of the lingual mucosa in 5 per cent of the cases. In 90 per cent glossitis was accompanied by cheilosis or angular stomatitis. Excretion of riboflavin in the urine was very low, 0.095 mg./100 ml. urine as against 0.350 mg. in a series of middle class pregnant women. The specificity of the observed signs was also therapeutically proved.

Dietary studies conducted at the same time among the Jewish population of Palestine[2–5] led to the conclusion that the diet, especially of the lower income groups, was very low in riboflavin. After the establishment of the State of Israel in 1948, the government accepted the advice of nutrition experts to enrich all flour milled in Israel with riboflavin, and at present flour is fortified with 2.5 mg. riboflavin, 2.5 gm. calcium carbonate and 30 gm. heat-processed soya meal per kg. The premix, consisting of soya meal, riboflavin and calcium carbonate, is prepared in one central mill and distributed to the other mills of the country. Preparation of the premix as well as its proper addition to the flour is controlled by the government.

The study here reported represents a clinical and biochemical resurvey of a population of pregnant women belonging to similar low income groups as were studied in the 1940's, in order to evaluate the effect of flour enrichment with riboflavin. Results of a dietary survey on these women will be reported elsewhere.

MATERIAL AND METHODS

Social Background of the Population Studied

The population studied in the 1940's represented a particular ethnic, social and economic group in an urban area which has remained almost unchanged and uninfluenced by the great changes that have taken place in Israel during the last eleven years. The present study was conducted on women living in the same quarters of Jerusalem and registered at the same Antenatal Care Stations, as in the previous study. The women were chosen by public health nurses who were acquainted with the economic and social conditions of the families. Only those women who lived under poor economic conditions and who had resided in Israel for at least seven years were included in our study. The low economic status of the population was reflected in the poor and crowded living conditions. More than 50 per cent of the women lived among families with three or more persons per room. The corresponding percentage of the total population of Jerusalem is 26.7.[6] Forty per cent of

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the women already had three or more living children.

The Group Studied

The group studied was comprised of about 400 women during the latter half of pregnancy or early lactation (one to three months after delivery). Most of them were examined twice or more, one-third of them only once. Thus, the total number of examinations approached 800 (Table I). Women taking riboflavin-containing preparations were excluded from the study.

TABLE I

Number of Women Examined

No. of Examinations	Clinical Examination		Urine Examination	
	No. of Women	No. of Examinations	No. of Women	No. of Samples
One	130	130	138	138
Two	189	378	159	318
Three	79	237	85	255
Four	14	56	13	52
Five	1	5	2	10
Total	413	806	397	773

Clinical and Biochemical Assessment

The clinical examination was restricted to a thorough inspection of the face, lips and tongue, since we intended to adhere to the same procedure which had been adopted in the previous survey. Similar principles held for the examination of riboflavin in the urine. As in the previous survey, urine specimens were obtained from the women on their visits to the station. Since single samples examined for riboflavin only provide a poor estimate of the average excretion,[7] the excretion per gram of creatinine was determined in order to obtain a higher degree of accuracy in the assessment of nutritional status with regard to riboflavin.[8] Riboflavin was determined fluorometrically[8] and creatinine according to the method of Taussky.[9]

RESULTS

Clinical Examinations

No case of typical ariboflavinosis with the characteristic symptoms of dyssebacea, cheilosis and glossitis was detected. Angular sto-

TABLE II

Number of Women Showing Papillitis and Angular Stomatitis in Relation to Living Conditions and Number of Living Children

	No. of Women	Per cent of Total	No. of Women Showing Signs of		
			Papillitis	Angular Stomatitis	Both Papillitis and Angular Stomatitis
No. of persons per room:					
0–2.9	192	46	2	1	—
3.0–5.9	152	37	1	8	1
6.0–8.9	54	13	—	3	—
9.0 and more	15	4	—	2	—
No. of living children:					
0	94	23	1	6	—
1–2	156	37	—	7	1
3–4	95	23	2	4	—
5–6	40	10	—	2	—
7 and more	28	7	—	3	—
Total	413	100	3	22	1

matitis was found in twenty-two cases and hypertrophic or atrophic papillae (papillitis) in three cases; one woman exhibited both symptoms (Tables II and III). Angular

TABLE III

Frequency of Papillitis and Angular Stomatitis by Months of Pregnancy and Early Lactation

	No. of Examinations	No. of Patients with		
		Papillitis	Angular Stomatitis	Both Papillitis and Angular Stomatitis
Month of pregnancy:				
IV	23	—	—	—
V	139	—	9	—
VI	141	—	7	—
VII	124	—	4	—
VIII	117	—	4	—
IX	78	1	6	1
Early lactation	178	2	1	—
Total	800	3	31	1

stomatitis, however, is not pathognomonic of riboflavin deficiency as was once thought. Furthermore, hyper- and atrophic papillae of the tongue may be attributed to dietary lack of one or another of the B vitamins.[10] The signs which were observed in a small number of cases are, therefore, of questionable value in the diagnosis of ariboflavinosis, when they are not accompanied by more typical symptoms, as were seen in the previous survey. There appeared to be no correlation between the frequency of these signs and the living conditions, the number of living children or the month of pregnancy (Tables II and III). In the previous survey, however, the largest number of cases occurred toward the last trimester of pregnancy. It may, therefore, be concluded that clear-cut clinical riboflavin deficiency essentially does not exist in the group studied.

Biochemical Examinations

These results were corroborated by those of riboflavin excretion studies (Table IV). Both mean and median values of riboflavin excretion per 100 ml. of urine were much higher in each month of pregnancy or in early lactation than the average of ariboflavinotic women in the previous study (9.5 μg./100 ml.) and were similar to the values obtained in normal control subjects (35 μg./100 ml.). Moreover, in much less than 10 per cent of the 773 examinations were values below 9.5 μg./100 ml. of urine. Mean and median riboflavin excretion per gram of creatinine were 0.47 and 0.43 mg., respectively. The riboflavin concentration of more than three-quarters of the samples was "high," that of 22 per cent "acceptable;" in only three samples (0.4 per cent) was the excretion "low." It is noteworthy that riboflavin excretion during early lactation appears to be higher than in pregnancy.

For purpose of comparison, twenty-four-hour excretion of riboflavin was examined in nineteen healthy male and female students and laboratory workers presumably subsisting on a satisfactory diet. Mean excretion was 511 (standard error: 61) μg./twenty-four hours or 53 (S.E.: 5.34) μg./100 ml. of urine or 0.44 (S.E.: 0.051) mg. per gram of creatinine.

COMMENTS

Our study shows that the ariboflavinosis which was widespread among pregnant women of the lower income classes in Jerusalem during the 1940's has now practically disappeared. It may be asked what role is played by flour enrichment with riboflavin in this remarkable improvement and what role by other factors, such as improvement of the economic situation, nutritional education and change of food habits, which may lead also to higher riboflavin intake. Obviously, one cannot answer this question with certainty. But since the population and the quarters studied remained stable from the sociologic point of view, and since the individuals studied belong to those lower income groups who cannot afford a diet rich in eggs, meat and milk products, it would appear reasonable to believe that the flour enrichment program was important in the improvement noted. Moreover, preliminary results of our dietary survey among these women (which we hope to publish

TABLE IV

Mean Values and Percentiles for Excretion of Riboflavin by Months of Pregnancy and Early Lactation

	Month of Pregnancy							
	IV (48) *	V (130)	VI (112)	VII (120)	VIII (116)	IX (82)	Early Lactation (165)	Total (773)
Riboflavin (μg./100 ml. urine)								
Mean	47	41	40	31	37	36	57	41
10th percentile	9	12	13	11	13	12	18	13
25th percentile	21	21	23	19	19	21	29	22
50th percentile	41	35	33	28	30	31	49	34
75th percentile	63	53	54	44	54	48	69	54
90th percentile	87	96	68	61	67	69	93	78
Riboflavin (mg./gm. creatinine)								
Mean	0.49	0.46	0.43	0.40	0.41	0.46	0.55	0.47
10th percentile	0.17	0.19	0.18	0.16	0.23	0.25	0.26	0.20
25th percentile	0.26	0.28	0.26	0.26	0.29	0.30	0.33	0.28
50th percentile	0.40	0.41	0.39	0.34	0.36	0.45	0.56	0.43
75th percentile	0.56	0.65	0.56	0.41	0.50	0.58	0.75	0.61
90th percentile	0.82	0.83	0.76	0.65	0.70	0.74	0.94	0.82
Results								
"Low" (less than 0.08 mg./gm.), per cent	—	0.8	0.9	—	0.9	—	—	0.4
"Acceptable" (0.08–0.27 mg./gm.), per cent	30.2	24.1	28.8	32.5	21.2	21.7	10.4	22.3
"High" (more than 0.27 mg./gm.), per cent	69.8	75.1	70.3	67.5	77.9	68.3	89.6	77.3

* Figures in parentheses represent number of samples.

extensively in the near future) show that about 35 per cent of the total riboflavin intake is derived from riboflavin added to the flour.

Riboflavin content was determined in fifty-seven samples of flour during the period of our study (October 1957 to January 1959). Twenty-nine samples were of "standard flour" (52 to 78 per cent extraction) used for "standard bread" and twenty-eight samples were of "white flour" (52 per cent extraction) used for white bread, rolls, cakes and macaroni. They contained 4.02 (standard error: 0.25) and 2.95 (0.19) mg. of riboflavin per kilogram.

Flour contributes significantly to the level of nutrition in Israel. According to the last Food Balance Sheet[11] covering the period from October 1956 to September 1957, the average quantity of cereals available amounted to 380 gm./person/day. Cereals, mainly wheat products, contributed 47 per cent of the calories, 51 per cent of the protein and 34 per cent of the riboflavin in the diet. Since flour is an inexpensive source of calories, its place in the diet of the lower income groups is of great importance. A recent survey conducted on 100 pregnant women living in development areas of Israel* has shown that 42 per cent of their total riboflavin intake is derived from flour products and 36 per cent from the riboflavin added to flour. Another

* Guggenheim, K. Unpublished results.

dietary survey performed in two agricultural settlements and comprising eighty-two households[12] has demonstrated that 0.68 mg. or 52 per cent of the average riboflavin consumption of 1.31 mg. per person is derived from cereals and 0.54 mg. or 41 per cent from flour fortification. Riboflavin intake from all foods available to the population amounted in 1956 to 1957 to 1.48 mg. per person.[11] In our study on nineteen adults, on the average 511 μg. of riboflavin were excreted per twenty-four hours. Adults subsisting for prolonged periods on diets providing 1.6 and 2.15 mg. riboflavin per day, respectively, have been shown to excrete 434 and 715 μg., respectively, per day.[13] It appears to follow from these figures that the persons studied by us may have consumed 1.5 to 1.8 mg. of riboflavin per day, the amount recommended by the National Research Council for male and female adults, respectively.[14]

The effect of flour enrichment on the health of the population was studied by Figueroa and co-workers.[15] These authors were impressed by the lack of avitaminosis among alcoholics examined in Chicago from June 1948 to July 1949, in contrast to its high incidence at the same place and in Boston in 1938 and 1941. A survey of the living conditions, food and alcohol consumption of the alcoholics showed no appreciable change between 1938 and 1948, the only factor being the enrichment of bread and cereals which started in Chicago in 1940 to 1941.

The principal study designed to evaluate the effect of flour enrichment on the health of a community was conducted in Newfoundland. At the time the study was begun in 1945 an extensive clinical and laboratory survey led to the conclusion that nutritional disease was widespread.[16,17] A resurvey[18] three years later, after enforced enrichment of wheat flour, showed considerable improvement in nutritional status. However, the authors of the study indicated a general improvement in economic status that had also occurrred during the study period. Although this factor of economic improvement cannot completely be excluded, it plays only a minor role in our study, since the population examined was selected from the lower social strata. It may, therefore, be concluded that flour enrichment with riboflavin has led to an improvement of nutrition and public health in Israel.

SUMMARY

A clinical and biochemical survey of 400 women during the latter half of pregnancy and early lactation, and belonging to the lower income strata of the Jewish population of Jerusalem, was performed in order to study their status of nutrition with regard to riboflavin. Clinically, no certain case of aribroflavinosis was found. Riboflavin examinations of 773 urine samples of these women showed "high" excretion in 77.3 per cent; "acceptable" excretion in 22.3 per cent, and "low" values in 0.4 per cent. In comparison to a similar survey conducted during the 1940's among pregnant women of similar social background, and living in the same quarters of Jerusalem, a considerable improvement has taken place. This is attributed mainly to the enrichment of flour with riboflavin.

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REFERENCES

1. Braun, K., Bromberg, Y. and Brzezinski, A. Riboflavin deficiency in pregnancy. *J. Obst. & Gynaec. Brit. Emp.*, 52: 3, 1945.
2. Bachi, R., Bavly, S. and Berman, S. V. Inquiry into poverty and malnutrition among the Jews of Jerusalem. Jerusalem, 1943. Hadassah Emergency Committee.
3. Bavly, S. Family Food Consumption in Palestine. New York, 1946. University of Columbia Press.
4. Cyderovitch, G. and Bavly, S. Inquiry into the living standard and nutrition among the Jewish urban population of Palestine. Jerusalem, 1947. Economic Research Institute of the Jewish Agency for Palestine.
5. Bergner-Rabinowitz, S. Hygiene, education and nutrition among Kurdish, Persian and Ashkenasic Jews in Jerusalem. Jerusalem, 1948. The Palestine Institute of Folklore and Ethnology.
6. Central Bureau of Statistics: Labor force survey. *Statist. Bull. Israel, Part A*, 9: 1128, 1958.

7. HEGSTED, D. M., GERSHOFF, S. N., TRULSON, M. F. and JOLLY, D. H. Variation in riboflavin excretion. *J. Nutrition*, 60: 581, 1956.
8. Interdepartmental Committee on Nutrition for National Defense: Manual for nutrition surveys, pp. 77, 120. Washington, D. C., 1957.
9. TAUSSKY, H. H. A microcolorimetric determination of creatine in urine by the Jaffe reaction. *J. Biol. Chem.*, 208: 853, 1954.
10. JOLLIFFE, N., TISDALL, F. F. and CANNON, P. R.: The clinical signs. In: Clinical Nutrition. Edited by JOLLIFFE, N., TISDALL, F. F. and CANNON, P. R. New York, 1950. Paul B. Hoeber, Inc.
11. Central Bureau of Statistics: Food balance sheet of Israel. *Statist. Bull. Israel, Part B*, 9: 851, 1958.
12. GUGGENHEIM, K. and DREYFUSS, F. Food habits and food consumption of Jews from Cochin in Israel. *Am. J. Clin. Nutrition*, 7:519, 1959.
13. HORWITT, M. K., HARVEY, C. C., HILLS, O. W. and LIEBERT, E. Correlation of urinary excretion of riboflavin with dietary intake and symptoms of ariboflavinosis. *J. Nutrition*, 41: 247, 1950.
14. National Research Council: Recommended Dietary Allowances, revised. Washington, D. C., 1958.
15. FIGUEROA, W. G., SARGENT, F., IMPERIALE, L., MOREY, G. R., PAYNTER, C. R., VORHAUS, L. J. and KARK, R. M. Lack of avitaminosis among alcoholics: its relation to fortification of cereal products and the general nutritional status of the population. *J. Clin. Nutrition*, 1: 179, 1953.
16. ADAMSON, J. D., JOLLIFFE, N., KRUSE, H. D., LOWRY, O. H., MOORE, P. E., PLATT, B. S., SEBRELL, W. H., TICE, J. W., TISDALL, F. F., WILDER, R. M. and ZAMECNIK, P. C. Medical survey of nutrition in Newfoundland. *Canad. M. A. J.*, 52: 227, 1945.
17. METCOFF, J., GOLDSMITH, G. A., MCQUEEN, A. J., DOVE, R. F., MCDEVITT, E., DOVE, M. A. and STARE, F. J. Nutritional survey in Norris Point, Newfoundland, *J. Lab. & Clin. Med.*, 30: 475, 1945.
18. AYKROYD, W. R., JOLLIFFE, N., LOWRY, O. H., MOORE, P. E., SEBRELL, W. H., SHANK, R. E., TISDALL, F. F., WILDER, R. M. and ZAMECNIK, P. C. Medical resurvey in Newfoundland in 1948. *Canad. M. A. J.*, 60: 329, 1948.