# PREVALENCE OF NUTRITIONAL DISEASE IN RURAL IRAN AND APPROACHES TO ITS ${\color{blue} \mathbf{CORRECTION}^1}$

John G. Reinhold<sup>2</sup>
(Invitational Paper<sup>3</sup>)

### ABSTRACT

Disturbances of calcium, iron, zinc and phosphorus metabolism occur with high frequencies in Iranian villages and are associated with the widespread development of nutritional diseases among children and women. Strong evidence has accumulated that consumption by villagers of large quantities of lightly baked bread made from wheaten wholemeals of total extraction, often without leaven or effective fermentation, is mainly responsible. Low intakes of vitamin D together with inadequate biosynthesis contribute, but D biosynthesis alone is incapable of overcoming the rachitogenic effects of the bread. Geophagia is sometimes a contributory factor. Measures for correcting the harmful effects of excessive consumption of bread are proposed.

### INTRODUCTION

Certain diseases caused by malnutrition afflict a high proportion of children and women living in the villages of Iran. Many infants develop rickets and as a result growth is

Contribution from the Medical Research Unit, Institute of Nuclear Medicine, Nemazee Hospital, and the Department of Biochemistry, College of Medicine, Pahlavi University, Shiraz, Iran.

<sup>2.</sup> Visiting Professor of Biochemistry, Department of Biochemistry, College of Medicine, Pahlavi University, Shiraz, Iran.

<sup>3.</sup> As with all invitational papers, this article has been subjected to minimum of change.

2

impaired, some develop disabling deformities and some may die. Osteomalacia (adult rickets) may cause severe disability in women. Malnutrition retards the growth and sexual development of adolescence and leaves some youths as sexually undeveloped dwarfs. Many women and children suffer from iron-deficiency anemia. For reasons that are not clear, perhaps because certain dietary essentials are lacking, the food consumption of villagers tends to be low. Decreased capacity for work and other energy-dependent activities result.

Studies of nutrition in villages of Fars conducted in the Institute of Nuclear Medicine of Pahlavi University and carried out during recent years strongly support the hypothesis that two main factors and a third of lesser importance are responsible for the development of nutritional disease by villagers. These are: (a) the consumption of large amounts of Lavash or Tanok (two common bread types in Fars) bread, often unleavened, made from wholemeals of 95 to 100% extraction rates, (b) insufficient exposure to sunlight and (c) geophagia.

Lavash and Tanok are rich in phytic acid (13) and fiber (J.G. Reinhold and M. Ghahramani, unpublished data), substances capable of causing rickets by interfering with the absorption of calcium and perhaps phosphorus from the intestine. They are also responsible for iron and zinc deficiency. Although the role of phytate has long been recognized we have recently shown that fiber interferes with the absorption of essential metals and is probably more important than phytate (15).

The village diet contains virtually no vitamin D and bodily needs must be satisfied by biosynthesis activated by sunlight. However, exposure to sunlight is avoided and is insufficient to support adequate synthesis of vitamin D. As a result, D deficiency develops. Geophagia is widely practiced and aggravates iron and zinc deficiency.

The faults of the village diet are correctible by: (a) Substitution of wholemeals of 80 to 90% extraction (like those used for much urban breadmaking) for the total extraction wholemeals. (b) Introduction of leaven and effective fermentation into village breadmaking. (c) Exposure of heads and forearms of infants, children, adolescents and women to not less than 15 min of full sunlight daily. (d) Incorporation of vitamin D into a staple food consumed by all villagers daily: (e) Provision of a vitamin D-fortified milk supplement daily to infants, children and adolescents. (f) Long-term efforts to promote milk,

meat, vegetable and fruit production and consumption so as to decrease the predominance of bread in the village diet. (g) Education regarding the harmful effects of geophagia.

The provision of the milk supplement recently introduced is a major step toward alleviation of malnutrition. However, the consumption of milk will not become fully effective unless enough vitamin D is provided in food or by biosynthesis to overcome the rachitogenic action of the high intakes of bread made from wholemeals of total extraction. The substitution of wholemeals of lower extraction for those now consumed will decrease the rachitogen intake. It will also decrease interference by wheat fiber with the utilization of protein, fat, essential trace elements and other indispensable nutrients. Implementation of all seven recommendations is necessary if the minimal nutritional needs of the rural population are to be satisfied.

Although our observations were made in villages of Fars, they apply also to other regions where locally produced wholemeals of total extraction are made into bread that serves as the predominant staple in the diet. They may apply also to certain segments of the urban population. Thus, rickets appears to be common in Isfahan (2).

## EVIDENCE FOR THE OCCURRENCE OF NUTRITIONAL DEFICIENCIES AND NUTRITIONAL DISEASE

Infantile rickets: A representative village, Ahmadabad, located north of Shiraz, was surveyed in the summer of 1352. Seventy-eight of its 94 infants between the ages of 6 and 24 months were examined including a subgroup of 31 by radiographic and biochemical techniques. Four of the latter showed active rickets. Twenty-six of the remaining 27 showed radiographic and/or biochemical as well as physical signs of rickets. Treatment with vitamin D caused remission (J.J. Cannell et al., unpublished data).

Osteomalacia: The most common complaint reported to physicians of the Pahlavi University Village Health Program is bone pain, a salient symptom of osteomalacia (A. Lahimgarzadeh, personal communication). Admissions to the University Hospitals include an appreciable number of village women with disability due to this often serious illness. Treatment with vitamin D has proved highly effective.

Hypogonadal dwarfism: First described in Shiraz in 1960 (11), hypogonadal dwarfism was

Iran. J. Agric. Res. Vol., 3, No. 1, 1975

Reinhold 4

shown to be the result of zinc deficiency (10). It is estimated that two to three per cent of male youths are affected to some extent in rural areas (18) and probably as many young females. Administration of zinc salts and a wholesome diet stimulates growth and sexual development of the affected dwarfs (5).

Iron deficiency anemia: One-third of village children below the age of 15 and one-fourth of village women have abnormally low hemoglobin concentrations in blood. The anemia responds to iron (4).

Low growth rates: Village infants after reaching ages three to six months fail to maintain growth rates prevailing in infants of Western countries or well-nourished infants in Iran (3,7).

Low food intakes: Food consumption of village boys is grossly inadequate (7) by accepted standards. The reason does not appear to be lack of food.

### CAUSES OF NUTRITIONAL DEFICIENCY AND DISEASE IN RURAL IRAN

Importance of wholemeal bread: The wheaten breads, Lavash or Tanok, made from wholemeals of total (95-100%) extraction make up 50 to 80% of the village dietary. These lightly baked, frequently unleavened breads contain between 0.5 and 1.3% phytate (13) and their content of fiber is high. Their consumption causes the metabolic balances of calcium, magnesium and zinc and often phosphorus to become negative; i.e., losses in the excreta exceed intakes (17). Retention of dietary nitrogen is decreased (K. Nasr and J.G. Reinhold, unpublished data). Concentrations of these elements, together with iron, in plasma fall below normal when Tanok is consumed (15). Claims that adaptation to phytate develops in a few weeks with return of calcium and magnesium balances to normal (20) if phytate consumption is prolonged, were shown by us to be inapplicable to the high intakes brought about by consumption of village bread (17).

Interference by Tanok with the absorption of these elements from the intestine exceeds that produced by phytate in similar amounts (17). We have found that wheat fiber sequesters zinc, iron and calcium and decreases their absorption (15). Indeed, Tanok from which all phytate has been removed has an increased ability to bind zinc, iron and calcium.

Fiber prepared from bran or Tanok also firmly binds all three metals (J.G. Reinhold *et al.*, unpublished data).

Effects of life-long consumption of Tanok: Calcium, zinc, phosphorus and nitrogen balances were measured in 13 adult villagers while they consumed a deit containing half as much phytate and fiber as had their village diets. High retentions of calcium (36%),zinc (27%) and phosphorus (23%) resulted (B.J. Campbell et al., unpublished data). Well nourished adults retain less than 3% of the amounts in similar diets. Retention of nitrogen was within this limit. The avidity with which the minerals were retained is evidence that bodily reserves are depleted. As a result, susceptibility to deficiency diseases becomes increased.

Vitamin D deficiency: Phytate is a known rachitogen (8) and its activity is reinforced by that of wheat fiber. Vitamin D overcomes the effects by increasing the efficiency of calcium and phosphorus absorption from the intestine. However, village folkways require that infants be protected against exposure to sunshine. Moreover, girls begin to wear veils at an early age and continue to do so through adolescence and womanhood. The resulting inadequacy of vitamin D biosynthesis together with absence of the vitamin from the diet leads to widespread deficiency among women and children with the high incidence of rickets and osteomalacia already mentioned (J.J. Cannell, unpublished data).

Geophagia: All of the more severely stunted zinc-deficient hypogonadal dwarfs have practiced geophagia (H.A. Ronaghy, personal communication). The clays consumed are calcareous and the high calcium intake that results interferes with phytate destruction in the intestine and also increases complex formation of phytate with zinc.

Other factors: The average number of pregnancies of village women is seven. Each pregnancy and ensuing lactation makes heavy demands upon calcium and phosphorus stores in bone. Village breads contain little available phosphorus (12). During periods when milk is not available, intakes of available phosphorus may be too low to maintain balance.

### RECOMMENDATIONS FOR CORRECTIVE ACTION

All of the mineral elements involved are present in the village dietary in amounts

that exceed requirements. Correction can be accomplished by improving their availability in the following ways:

Lowering the rate of extraction of wholemeals: The change need be only from 95-100% to 80-90%. However, to accomplish this probably requires replacement of the currently used primitive village mills by sophisticated equipment capable of separating offal from flour. Patwardhan's (9) and our own experience indicate that sifting of stoneground meals is incapable of lowering the rate of extraction below 95%. The cost and complexity of new mills will make necessary their location in regional centers. On the other hand, centralized production would facilitate incorporation of vitamin D supplements into the flour. Existing mills in cities could supply part of the need by expanded operations.

Introduction of leaven into village breadmaking: We have shown that fermentation of wholemeals by yeast improves the availability of zinc several-fold (12). The studies were carried out by use of radioactive zinc 65-labeled wheat. The label was introduced during the period of maturation to assure that the behavior of naturally occurring wheat would be accurately reproduced. The destruction of phytate by fermentation is more effective in wholemeals of less than total extraction rate (12). Some village breadmakers already use a sourdough leaven. However, with rare exceptions, the length and conditions of fermentation are not conducive to the fermentative changes that improve availability. Properly used leaven yields breads that are indistinguishable from traditional unleavened breads in flavor and appearance. Thus, acceptance of leavened bread should not create difficulties.

Increased exposure to sunshine to promote vitamin D synthesis: A concerted campaign of education by members of the Health Corps and others should persuade parents that 15 min of sunshine daily will improve the health of children and themselves without causing their complexions to be darkened to an undesirable extent. However, biosynthesis of vitamin D, even when maximal is incapable of restoring calcium metabolism to normal if consumption of bread continues to be excessive (B.J.Campbell et al., unpublished data).

Incorporation of vitamin D supplements into the diet: As additional protection against rickets and osteomalacia, vitamin D should be incorporated into the wholemeals ground in regional centers. Five hundred I.U./kg is suggested. At this rate, no person is likely to

Iran. J. Agric. Res. Vol. 3, No. 1, 1975

Reinhold 7

ingest more than 400 I.U. daily and harmful excesses will be avoided. To provide the balance of the daily requirement of children, it would be desirable to include vitamin D in milk provided in schools.

Supplementary milk: The program now being planned under governmental auspices is essential for adequate nutrition of children from weaning through adolescence. It will correct suboptimal intakes of amino acids as well as of minerals.

Increased milk, meat, vegetable and fruit production: An increase in supply and consumption in villages of a variety of foods is necessary if dependence upon bread is to be decreased. Decreasing the monotony of the diet may improve food intake.

Geophagia: Health Corps members could publicize the harmful effects of geophagia. However, since unfulfilled dietary needs are probably important in its etiology, improvement of the village diet resulting from the measures recommended should diminish the craving for clay.

#### APPROACHES THAT HAVE PROVED INEFFECTIVE

Supplementation of the village diet with zinc requires long periods of treatment and relatively large dosages to produce what is at best a limited response (19, M. Mahloudji et al., unpublished data). Although the response to supplementation with iron is more effective (4) neither iron nor zinc supplements should be necessary once the proposed modifications of the diet are introduced.

The proteins of bread contain insufficient lysine and methionine for optimal nutrition. Since other sources are limited, deficiencies of these amino acids have been postulated (7). However, supplementation of village diets with lysine is not followed by increased rate of growth (6) or other major benefits.

### **ACKNOWLEDGEMENTS**

The studies described were carried out with the participation of members of the Departments of Biochemistry, Community Medicine, Medicine, Pediatrics and Radiology of the College of Medicine and of Food Technology and Nutrition and Soil Science of the

Iran. J. Agric. Res. Vol. 3, No.1, 1975

College of Agriculture of Pahlavi University, Shiraz, Iran.

This work was supported by grants from the following:

Agency for International Development, Washington, D.C. through Contract HSM-110-69-435 and by Contract CCD-69-53 between the University of Pennsylvania and the Nutrtion Program, Center for Disease Control, HSMHA, Atlanta, Georgia.

The Nutrition Foundation, Inc., New York, N.Y.

The Research Council of Pahlavi University, Shiraz, Iran.

### LITERATURE CITED

- 1. Amirhakimi, G.H. 1974. Growth from birth to two years of rich urban and poor rural Iranian children compared with Western norms. Ann. Human Biol. 1: 427-442.
- Emami, A.R., H. Hedayat, H. Khayambashi, G. Motamedi, F. Hekmatyar, M. Khezri and A. Bouroumond. 1970. Incidence of rickets among school children in Isfahan. Pahlavi Med. J. 1: 63.
- 3. Eminians, J., G.H. Amirhakimi and M. Mahloudji. 1972. Health status of infants in a small village community near Shiraz, Iran. J. Trop. Paed. 18:11-15.
- Haghshenass, M., M. Mahloudji, J.G. Reinhold and N. Mohammadi. 1972. Iron-deficiency anemia in an Iranian population associated with high intakes of iron. Amer. J. Clin. Nutr. 25: 1143-1146.
- Halsted, J.A., H.A. Ronaghy, P. Abadi, M. Haghshenass, G.H. Amirhakimi, R.M. Barakat and J.G. Reinhold. 1972. Zinc deficiency in man: The Shiraz experiment. Amer. J. Med. 53: 277-284.
- Hedayat, H., H. Shahbazi, R. Payan, M. Azar, M. Bavendi and G. Donoso. 1973. The
  effect of lysine fortification of Iranian bread upon nutritional status of school children
  Acta. Paed. Scand. 62: 297-303.
- 7. Maleki, M. 1973. Food consumption and nutritional status of 13 year old village and city schoolboys in Fars Province, Iran. Ecol. Food Nutr. 2: 39-42.
- 8. Mellanby, E. 1949. Rickets-producing and anticalcifying action of phytate. J. Physiol. 109: 448-533.
- 9. Patwardhan, V.N. 1952. Nutrition in India. Bombay.
- Prasad, A.S., A. Miale, Jr., Z. Farid, H.H. Sandstead, A.R. Schulert and W.J. Darby.
   1963. Biochemical studies on dwarfism, hypogonadism, and anemia. Arch. Int. Med.
   111: 407-428.

- Prasad, A.S., J.A. Halsted and M. Nadimi. 1961. Syndrome of iron deficiency, anemia, hepatosplenomegaly, hypogonadism, dwarfism and geophagia. Amer. J. Med. 31: 532-546.
- 12. Reinhold, J.G. 1975. Destruction of phytate in wheaten wholemeals of high extraction rate by fermentation with yeast. J.Amer. Diet. Assoc. 66 (in press).
- 13. Reinhold, J.G. 1972. Phytate content of leavened and unleavened Iranian breads. Ecol. Food. Nutr. 1: 187-192.
- 14. Reinhold, J.G. A. Parsa, N. Karimian, J.W. Hammick and F. Ismail-Beigi. 1974. Availability of zinc in leavened and unleavened wholemeal wheaten breads as measured by solubility and uptake by rat intestine in vitro. J. Nutr. 104: 976-982.
- 15. Reinhold, J.G. B. Faradji, P. Abadi and F. Ismail-Beigi. 1975. Binding of zinc to fiber and other solids of wholemeal bread, with a preliminary examination of the effects of cellulose consumption upon the metabolism of zinc, calcium, and phosphorus in man. In Trace Elements in Human Disease. Edited by A.S. Prasad and D. Oberleas. Academic Press, New York.
- 16. Reinhold, J.G., H. Hedayati, A. Lahimgarzadeh and K. Nasr. 1973. Zinc, calcium, phosphorus, and nitrogen balances of Iranian villagers following a change from phytaterich to phytate-poor diets. Ecol. Food Nutr. 2: 157-162.
- Reinhold, J.G., K. Nasr., A. Lahimgarzadeh and H. Hedayati. 1973. Effects of purified phytate and phytate-rich bread upon metabolism of zince, calcium, phosphorus and nitrogen in man. Lancet 1: 283-288.
- 18. Ronaghy, H.A. 1970. Growth retardation as a factor in rejection from military service in the Shiraz area. Pahlavi Med. J. 1: 29.
- Ronaghy, H.A., J.G. Reinhold, M. Mahloudji, P. Ghavami, M.R. Spivey-Fox and J. A. Halsted. 1974. Zinc supplementation of malnourished schoolboys in Iran; increased growth and other effects. Amer. J. Clin. Nutr. 27: 112-121.
- Walker, A.R.P., J.T. Irving and F.W. Fox. 1948. Studies on human mineral metabolism.
   The effect of bread rich in phytin phosphorus on metabolism of certain mineral salts with special reference to calcium. Biochem. J. 42: 452-462.