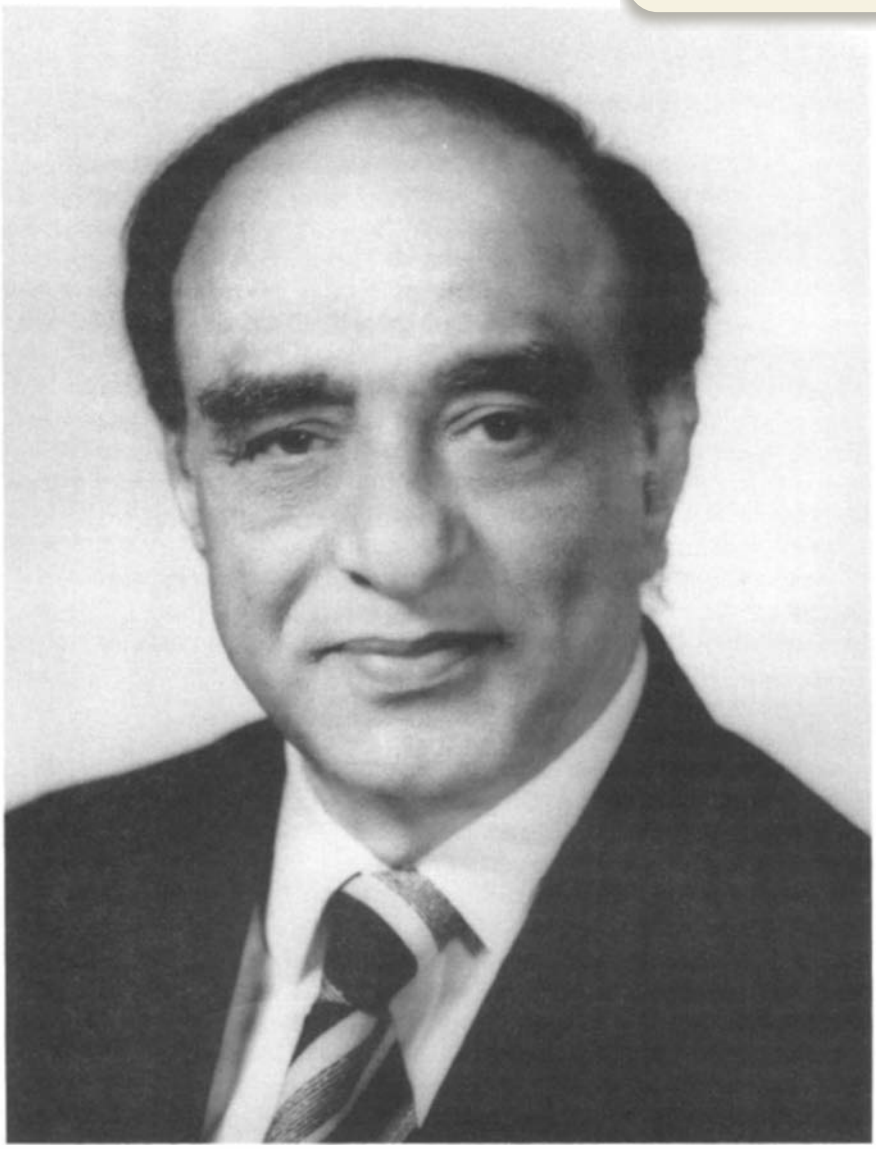

Annu. Rev. Nutr. 1992. 12:1–17

THE CONTRIBUTION OF NUTRITION RESEARCH TO THE CONTROL OF UNDERNUTRITION: The Indian Experience

C. Gopalan

Nutrition Foundation of India, B-37 Gulmohar Park, New Delhi 110 049, India

KEY WORDS: nutritional deficiency diseases of India, protein-energy malnutrition, hypovitaminosis A, pellagra, fluorosis, lathyrism

---

CONTENTS

0199-9885/92/0715-0001$02.00

INTRODUCTION

The eradication of undernutrition in developing countries can only be achieved through socioeconomic development and the elimination of poverty. But this consideration should in no way obscure the urgent need for scientific research in human nutrition and the important practical contributions that such research can offer. In India, as in all developing countries, a wide spectrum of specific nutritional deficiency diseases is found; the precise pathogenesis and approach to the prevention of each of these diseases needs careful elucidation.

Scientific research in India on problems of undernutrition during the last three decades has helped generate several practical methods of action. These contributions have also enriched nutrition science in general. Some of the recent developments are briefly discussed below. What follows is by no means a comprehensive catalogue of notable nutrition research contributions from India but only selected examples that have a direct bearing on major nutritional diseases encountered in the country today.

MAJOR NUTRITIONAL PROBLEMS

The outstanding nutritional problems in the country that currently account for significant impairment of the country's human resources are protein-energy malnutrition (PEM), which leads to physical and mental retardation and underdevelopment of several thousands of children; vitamin A deficiency, which results in keratomalacia and nutritional blindness; widespread iron-deficiency anemia, which impairs productivity and increases the vulnerability of poor populations to infections; and endemic goiter and other iodine-deficiency manifestations, which affect physical growth and mental development.

Other nutritional problems are somewhat more limited in distribution but, nevertheless, present fascinating challenges to biologists and health scientists: pellagra in the Deccan plateau, fluorosis in some parts of the country, lathyrism in Central India, and "lactose intolerance."

PROTEIN-ENERGY MALNUTRITION

Protein energy malnutrition (PEM) has held the central stage in global nutrition research for nearly three decades. Numerous studies have been published on this subject in India, but we highlight two important Indian contributions that have helped to bring about a major change in prevailing perceptions regarding its pathogenesis and approaches to its prevention.

The first was the clear demonstration that the primary dietary problem underlying PEM in India was *not* a deficiency of protein (as was hitherto

widely claimed) but rather a deficiency of calories (21). Careful surveys of diets of children under five years of age in different parts of the country in communities where PEM was common showed that the daily protein intake ranged from 2.8 g/kg body weight to 1.7 g/kg—levels that on the basis of widely accepted international and national recommendations could be considered adequate. The daily calorie intakes, however, were of the order of 70 to 75 kcal/kg versus the figure of 100 kcal/kg, which is generally considered adequate. While the diets of over 90% of children were deficient in calories, the diets of only 35% of the children were deficient in protein. And if food intake had been raised to meet the calorie requirements of the latter group of children, their protein needs would have been met. Practically no situation was found in which the children's diets were adequate in calories but deficient in protein alone (30).

That the calorie gap in the prevailing diets of children of poor communities was the crucial factor was further demonstrated in yet another longitudinal study (of 14 months) (33) of a community of poor children whose daily diets provided no more than 700 kcal (with 18 g protein). This study showed that when the calorie gap in these diets was bridged by supplementation with 300 additional kcal daily, derived from ("empty calories") carbohydrate and fat sources (wheat flour, sugar, and edible oil) with little additional protein (no more than 3 g), growth performance was significantly improved and clinical manifestations of PEM were averted.

These findings indicated that the prevailing emphasis on "the protein gap" and "protein concentrates" was wholly misplaced; and that the solution to the problem of PEM fortunately need not depend on imports of expensive protein-rich concentrates but rather could be achieved through proper use of inexpensive traditional cereal-legume-based diets within the economic reach of poor families and within the country's resources.

The Practical Challenges

The real challenge in the prevention of PEM is to ensure that children under five years of age (especially under three years) get their habitual cereal-legume-vegetable foods in amounts adequate to meet their calorie needs. A hurdle in feeding cereal-legume-based diets to very young children stems from the low calorie-density of these diets, "the bulk factor." Research in India has also attempted to address this issue and to identify traditional home-based techniques through which this bulk factor can be overcome, the viscosity of cooked cereal foods can be reduced, and their calorie density increased (15, 34).

We now proceed to the second major contribution to the understanding of the PEM problem. It is well recognized that two distinct clinical syndromes are associated with PEM, namely kwashiorkor and marasmus. (Marasmus in early infancy associated with highly inadequate intakes of milk has to be

considered as a separate category. Here we address marasmus in the preschool child.) At any given point of time throughout the 1960s and 1970s one could calculate on the basis of available survey data that while roughly about 1% of children under three years of age in poor communities may exhibit kwashiorkor, nearly 2 to 3% may show marasmus. Thus, at a given point of time, in the 1960s and 1970s in poor communities we could expect to see several thousands of poor children suffering from kwashiorkor and several thousands more suffering from marasmus, both of these conditions existing almost side by side in the same villages.

The earlier widely held postulate was that these two manifestations were different diseases with entirely different dietary etiologies: kwashiorkor was thought to be due primarily to "protein deficiency and calorie excess" while marasmus was thought to be due to calorie deficiency. If this was really the case, poor developing countries like India would have had on their hands two major public health problems requiring two entirely different approaches to their prevention and control. Studies carried out in India led to the conclusion that this fortunately was not the case.

A major clarification of immense practical significance was that kwashiorkor and marasmus are *not* two different diseases but just two facets (clinical manifestations) of one and the same central problem of PEM, with a common dietary etiology, and therefore requiring identical approaches for their solution.

On the basis of intensive studies of the actual diets and hormonal profiles of children suffering from these two syndromes, it was postulated that marasmus represents the stage of attempted "adaptation" to the nutritional stress. Thus hormonal mechanisms are invoked to ensure that the integrity of highly vulnerable tissues with a high protein-turnover, like the liver, pancreas, and viscera, is maintained at the expense of the muscle (21). Kwashiorkor represents the stage when this adaptation breaks down. Further studies helped to elucidate the probable nature of the hormonal changes that may be involved in such an adaptation mechanism leading to marasmus at one stage of the disease and to a breakdown of adaptation leading to kwashiorkor at a later stage (35, 36). Thus in marasmus, elevation of plasma cortisol levels was found to be of a higher order than in kwashiorkor; the adrenal cortical response to injection of corticotrophin was exaggerated. Plasma growth hormone levels and their response to stimuli that were found to be raised in kwashiorkor were not altered in marasmus. Plasma somatomedin activity was found to be low in kwashiorkor but not in marasmus.

These hormonal changes may help to ensure that in the face of stress posed by nutritional deprivation, muscle tissue is preferentially broken down so that the structural and functional integrity of more vital tissues like the liver, pancreas, and viscera is maintained. Marasmus may thus be looked upon as

an extreme stage of adaptation—the farthest limit of what was described as a "contraction of the metabolic frontiers." When adaptation eventually breaks down because of continued stress or its aggravation by additional factors like fresh infections, etc, the fatty infiltration of liver, a fall in serum albumin, a reduction in serum enzymes, and edema ensue with the resultant picture of kwashiorkor. The fact that marasmus and kwashiorkor exist side by side in the same community subsisting on the same diet, as well as the fact that marasmus and kwashiorkor can exist *in the same child* at different points of time, lends support to the postulate that the two syndromes are but two facets of one and the same disease.

This clarification has helped place the entire problem of marasmus and kwashiokor in proper perspective as far as the public health approach to these diseases is concerned. It became clear that we were dealing with two manifestations of a *single* problem and that we did not need two divergent strategies for their control. It is hardly necessary to emphasize here the far-reaching practical implications of this conclusion.

The extensive work done on the foregoing and other aspects of the problem of PEM in India in the 1950s and 1960s has been reviewed in an earlier publication (62).

Misuse of the Term Adaptation

In the above discussion the term *adaptation* has been used to refer to the organism's response to stress. It is, however, important to emphasize that "adaptation" as used here is not synonymous with normalcy and therefore something that is "acceptable." Even a severely marasmic child with extreme emaciation but a normal liver is "adapted"! I emphasize this point because of the loose manner in which the term *adaptation* is now being misused to propagate the view that stunting and "moderate malnutrition" (which are not of such severity as to be life threatening) arising from PEM in Third World children may be viewed as an acceptable adaptation, consistent with their "culture" and environment.

In several recent publications (23–25, 27, 28) I have cautioned against the danger of the misuse of the concept of adaptation in a manner likely to promote social and political indifference to (and acquiescence in) "moderate malnutrition" in children.

Outstanding Indian contributions bearing on the question of "adaptation" to chronic energy deficit, and on the functional significance of small body size, are those of Shetty (59) and Satyanarayana et al (55–58). These authors emphasize the point that while small body size and behavioral alterations in work patterns arising from chronic energy deficit may facilitate survival under marginal living conditions, they cannot be viewed as beneficial satisfactory adaptive responses consistent with optimal levels of productivity

and quality of life. Physical activity, especially with respect to moderate and strenuous work, is compromised in subjects with low body weight and poor muscle mass (55, 56), and there is no convincing evidence of increased metabolic efficiency with respect to energy handling by the residual active tissues of the body in chronically energy deficient small-sized individuals (59).

KERATOMALACIA AND NUTRITIONAL BLINDNESS

The current global approach to the prevention of keratomalacia arising primarily from vitamin A deficiency is to distribute two massive annual oral doses of synthetic vitamin A, one each at six-month intervals, to children under three years of age. This approach was developed and pioneered in India on the basis of experimental, clinical, and field studies. That vitamin A can be stored in the liver for prolonged periods and is released gradually to meet tissue needs has long been well-established. It was important, however, (*a*) to establish an optimal dosage of vitamin A that while not being toxic would adequately protect children against keratomalacia for fairly long durations; (*b*) to identify the most effective and feasible route and form of administration of the vitamin, (*c*) to demonstrate that under real-life conditions in the field, the administration of vitamin A in the dosage, frequency, and form identified above helps raise and maintain serum vitamin A levels in children over several months and thus does in fact offer protection against keratomalacia, and finally (*d*) to develop a practical procedure for the routine evaluation of the program by the public health agency.

Development of the Massive Dose Prophylaxis Approach

An indication of the extensive amount of work that was involved in the development of this prophylaxis program can be obtained from the following brief account of the study that preceded the introduction of this program in the National Health System.

CHOICE OF PREPARATION In a preliminary trial in which a single dose of 300,000 IU of vitamin A was given orally as a water-immiscible preparation to a group of preschool children, 25% developed signs of acute though transient vitamin A toxicity characterized by raised intracranial tension (bulging fontanelles), restlessness, and fever (63). When the same amount was given as an oil-soluble preparation, the incidence of toxic signs was 4%. Moreover, animal studies had earlier shown that the best hepatic storage was achieved with oral administration of oil-soluble vitamin A (52). Therefore an oil-soluble preparation was chosen. Oral administration of 100,000 IU of oily vitamin A produced significant increases in serum vitamin A levels, but the

same dose given intramuscularly had no such effect because much of the vitamin continued to remain at the site of infection (52). Oral dosage was therefore preferred; in addition, it was a more convenient method of administration.

OPTIMAL DOSAGE LEVEL Longitudinal studies on groups of children showed that a single oral dose of 300,000 IU was able to sustain normal levels of serum vitamin A in children for a period of 6 months. Studies in which 200,000 IU of vitamin A were given along with labelled retinyl acetate (urinary excretion of the label was monitored) indicated that 70% of the dose was absorbed and somewhat less than 50% of the total dose was retained (51). The fact that urinary excretion of lysosomal enzymes arylsulphatase and acid phosphatase showed either no increase or an insignificant transient increase following the administration of such a massive dose demonstrated that lysosomal damage was not significant (49).

The real test of the efficacy of this prophylaxis approach was demonstrated by a prolonged 5-year field trial in which 2500 children under five years of age and drawn from several villages received 300,000 IU of vitamin A administered orally once a year for a period of 5 years. This study showed (*a*) a 75% reduction in the overall incidence of vitamin A deficiency in the community, (*b*) that no new cases of keratomalacia occurred during this period, and (*c*) serum vitamin A levels were consistently higher in children who received the dose than in children who had not (64).

After these extensive, time-consuming tests were completed, scientists advised the Government of India to include this program as part of routine primary health care in at least nine states of the Indian Union where evidence indicated that vitamin A deficiency was widely prevalent.

As a precautionary measure in order to reduce the risk of toxicity to the absolute minimum, it was also recommended that the dose be reduced to 200,000 IU and that it be given twice a year at six-month intervals. A practical simple method that was feasible under field conditions for evaluation of the implementation of the program was also developed (65).

This may seem to be an unqualified success story. However, looking back on these efforts that were initiated a quarter of a century ago, and now looking at the results, we may legitimately ask whether all the expectations that prompted these efforts by Indian nutrition scientists have in fact been fulfilled.

The control of nutritional blindness through the "short-cut" of administering synthetic vitamin A had been envisaged as a short-term approach—not as the permanent solution to the problem. It was always recognized that the ultimate solution lay in the promotion of the optimal use of β-carotene-rich foods, green leafy vegetables, in the diets of poor children. Unfortunately, the

euphoria and complacency created by the introduction of the prophylaxis through massive dosage of synthetic vitamin A have to a considerable extent retarded research designed to develop and promote the better use of inexpensive β-carotene-rich foods in the country. If such research has not altogether come to a standstill, it is proceeding, at best, at a snail's pace as a program of low priority.

Secondly, implementation of the prophylaxis program is obviously slow, especially in states like Bihar. Most disconcerting is the fact that we do not have any authentic indication of what real impact the prophylaxis program has had on nutritonal blindness. The official figures of the annual incidence of cases of nutritional blindness will not stand scientific scrutiny. We do not even seem to have reliable data on changes in the annual incidence of keratomalacia in our leading ophthalmic and pediatric hospitals since the introduction of the program. In the absence of such data, we are in no position to counter or confirm the claims that are frequently made.

IRON DEFICIENCY ANEMIA

A major contribution of immense practical value has been the development of a technique for the fortification of common salt with iron. This research was not just a simple exercise in food technology but included studies of bioavailability and field trials to determine acceptability and efficacy.

Contrary to the general belief that iron deficiency anemia is mostly a disease of women in the reproductive age group, studies carried out under the auspices of the Indian Council of Medical Research showed that it is also very much a disease of preschool children and indeed even of adult men. A more recent study by the National Institute of Nutrition (47) showed that 65% of adult women, 75% of pregnant women, 77% of preschool children, and nearly 45% of adult men in poor rural communities were anemic. Anemia is probably the most extensive nutritional deficiency disorder in the country. Recent research indicates that apart from impairing productivity, the disease also has other functional implications. Though Indian diets generally provide 20 to 30 mg of iron daily, because of their high phytate content owing to the predominance of cereals, the bioavailability of dietary iron as determined by radioisotope technique is only 1 to 5%.

Iron Fortification

The rational ultimate answer to the problem would, of course, consist in the diversification and improvement of diets—a goal likely to take many years to achieve. The program of distribution of iron-folate tablets though the health system can reach only a small proportion of the population. Under the circumstances, a sensible practical approach would be to increase intake of iron through fortification of a suitable dietary item. Since common salt is a

food commodity in universal use and since the poor take it in almost the same amounts as the rich, common salt was the obvious suitable candidate for iron fortification.

THE FORMULA The challenge was to identify a formula for fortification that would satisfy the conflicting requirements of stability, acceptability, and bioavailability. The formula identified by the National Institute of Nutrition as satisfying these requirements consisted of ferro orthophosphate (3.5 g per kg) and sodium acid sulphate (5 g per kg) as an absorption promoter and provided 1 mg iron per gram of salt. Later this formula was further improved by replacing ferric phosphate with much less expensive ferrous sulphate (3500 ppm) and orthophosphoric acid or sodium orthophosphate (2800 ppm). With an estimated intake of 15 g of common salt per adult per day, common salt fortified as noted above will provide an additional 15 mg of iron.

FIELD STUDIES The acceptability and efficacy of salt fortified as above was investigated through a field trial lasting for 18 months among 1600 (boys and girls) school children between 5 and 15 years of age who were divided into two matched groups, one receiving fortified salt and the other unfortified salt. The culinary acceptability and physiological efficacy of the fortification procedure were clearly demonstrated (47). Subsequently, a multicentric study coordinated by the National Institute of Nutrition and covering a population of 6000 was also undertaken. In this study the salt was made available to the population through the regular food distribution system. Analysis of data on hemoglobin levels in the experimental and control group again helped to confirm the significant impact of the procedure on the anemia problem (53). The government of India has now been persuaded to undertake this program initially in some parts of the country.

A major hurdle was the need to ensure that the fortification of common salt with iron was compatible with the government's decision to support the universal iodation of common salt intended for human consumption in the country as a method of prevention and control of endemic goiter. Scientists of the National Institute of Nutrition recently developed a feasible procedure for the simultaneous fortification of common salt with iron and iodine.

ENDEMIC GOITER

According to some estimates more than 40 million people in the country suffer from goiter. The National Goiter Program based on iodation of common salt was initiated in the latter half of the 1950s, but after an initial promising start had languished because of poor implementation and inept supervision (22). The emergence of new goiter-endemic areas has added fresh dimensions to the problem (2).

Recent studies from India have provided important indications of hitherto unsuspected serious dimensions of the problem of neonatal chemical hypothyroidism (NCH) in endemic goiter zones (37, 39). As high as 13% of neonates in endemic goiter areas have been shown to be functionally decompensated on the basis of T4 and TSH levels in their cord blood as determined by radioimmunoassays techniques. This observation corresponds closely to the finding of a study under the auspices of the Nutrition Foundation of India that nearly 15% of school children investigated in endemic goiter districts showed evidence of varying degrees of mental underdevelopment. These findings have lent urgency and importance to our National Goiter Control Program, which has yet to achieve its full potential. A somewhat complacent view of the role of iodine deficiency in mental underdevelopment had been taken earlier because of the very low incidence of cretinism and deaf mutism in the endemic goiter zone.

Parenteral administration of iodized oil to pregnant women is now being promoted in some quarters as a suitable prophylactic approach in relatively inaccessible areas until such time as the salt iodation program gathers full momentum. Recent Indian studies (38), however, sound a note of caution against resorting to this approach. According to these studies, iodized oil injections, when given to mothers particularly in the last trimester of pregnancy, do *not* help to reduce the incidence of neonatal chemical hypothyroidism; the relevance or even the safety of administering iodized oils to pregnant mothers has been seriously questioned. These views have been challenged, and apparently some controversy exists. Clearly, however, it would not be prudent to push ahead with any procedure regarding whose safety serious doubts have been expressed, especially when a time-tested, safe, and inexpensive alternative (salt iodation) is already available.

The foregoing account deals with major nutritional deficiency disorders affecting vast numbers of the country's population. A brief account now follows of scientific contributions from India towards the better understanding of four other nutritional disorders that, although not as extensive as those described earlier, are of considerable interest to health and nutrition scientists all over the world.

PELLAGRA

Pellagra is a classical nutritional deficiency disorder traditionally associated with poor populations whose staple is maize (corn). The low content in maize of the essential amino acid tryptophan, the precursor of nicotinic acid, has been generally held responsible. The important finding from India, which ran clearly counter to this well-accepted view, was that endemic pellagra in the Deccan plateau of India occurred in populations subsisting not on maize but on the millet sorghum (jowar), which is *not* poor in tryptophan. A feature

common to both maize and sorghum, however, is the high content of the amino acid leucine. This finding sparked a new series of studies on pellagra, starting with a paper (32) in which we proposed that the high level of leucine in sorghum may play a positive role in the pathogenesis of the disease. Subsequent studies showed that excess leucine in otherwise poor diets could induce disturbances in the tryptophan—niacin pathway, which were reflected in increased urinary excretion of quinolinic acid on leucine feeding (11), a decreased rate of synthesis of nicotinamide nucleotides by erythrocytes (48), decreased activity of quinolinate phosphoribosyl transferase (QPRT), a key enzyme in NAD synthesis in liver (10), and a fall in platelet 5-hydroxytryptamine levels (43).

These studies showed that excess leucine in poor sorghum diets could bring about significant changes in key enzymes in the tryptophan-niacin pathway that ultimately resulted in decreased nicotinamide nucleotide formation from dietary tryptophan and thus led to conditioned deficiency of nicotinic acid.

Further studies showed that these effects of excess leucine could be countered by pyridoxine. Posttryptophan load excretion of xanthurenic acid, kynurenic acid, and quinolinic acid, which were initially raised in pellagrins, were reduced after pyridoxin treatment (42).

Thus the Indian studies indicate that in the pathogenesis of pellagra (which is by no means exclusively confined to maize eaters but can also occur in sorghum eaters), apart from tryptophan deficiency (in maize eaters), an excess of leucine (in sorghum eaters) and deficiencies of pyridoxin and nicotinic acid (in both maize eaters and sorghum eaters) may all play a part. The above observations on the possible role of leucine in pellagra have been contested and challenged by some scientists from Europe and the United States. Some recent reports from England, however, have lent support to the observations from India. Magboul & Bender (44) showed that diets that provide excess leucine brought about a "significant reduction in the concentrations of nicotinamide nucleotides in liver and blood." The effect was only apparent when the diets provided less than adequate amounts of nicotinamide. The addition of leucine was also shown to bring about "significant activation of tryptophan oxygenase and inhibition of kynurenase." In a subsequent communication Bender (12) reported that "dietary excess of leucine led to inhibition of kyureninase and increased the activity of piconilate carboxylase—which could be expected to explain decreased synthesis of nicotinamide nucleotides."

LATHYRISM

Neurolathyrism characterized by spastic paraplegia affecting the lower extremities is an ancient disease and is endemic in areas in which diets are predominantly based on the pulse *Lathyrus sativus*. Though the association of

lathyrism with the consumption of the pulse has been known for over a century, the toxic factor in the pulse responsible for the disease could not be identified, mainly because the disease could not be reproduced in experimental animals.

A major breakthrough was achieved at the National Institute of Nutrition (54) when it was demonstrated that alcoholic extracts of lathyrus sativus could produce neurotoxic manifestations when injected into baby chickens. The toxic factor was subsequently isolated and identified as BOAA (B-oxalyl aminoalanine) (1, 46). A simple household method by which the toxin can be completely removed from the seed by steeping the seeds in hot water for about an hour, or by parboiling the seed in a process similar to the parboiling of rice, was also developed (45). Simultaneously, attempts were also made by agricultural scientists in India to identify and selectively propagate genetic strains of lathyrus sativus low in BOAA. These attempts were not successful, but recently new attempts have been made in other parts of the world (Canada).

Thus far, the scientific research efforts that have gone into the elucidation of the problem of lathyrism have not directly resulted in the eradication of the disease. Attempts to ban the cultivation of the offending crop failed because the crop is hardy and able to grow on unirrigated land; it has been the staple of the poor and there was no easy substitute. Recently, however, following the relative decline in production of pulses in the wake of the green revolution, *Lathyrus sativus* has found a flourishing market as an adulterant of other more expensive pulses like Bengal gram and reportedly is being widely exported out of the endemic zone for this purpose (26). To the extent to which these new developments dictated by commercial considerations reduce sole reliance by the poor of the endemic regions on *Lathyrus sativus* as their staple food, they may be of some benefit, but if the profitability of adulteration should act as an incentive for intensive cultivation of *Lathyrus sativus,* the problem would be disseminated well beyond the present "endemic" zones.

FLUOROSIS

While in other parts of the world, there is active support for the fluoridation of water as a method for the prevention of dental caries, in India the problem in some parts of the country (especially Panjab and Andhra Pradesh) is the presence of excess fluoride in drinking water that leads to skeletal changes—sometimes so severe as to be incapacitating.

Endemic fluorosis was in fact first identified in the country in some areas of the present Andhra Pradesh that were then parts of the erstwhile Madras Presidency (60). Subsequently, endemic fluorosis belts were also identified in Punjab (61). The disease affects the rural poor in areas where the drinking water may contain as high as 15 ppm of fluoride. While attempts to de-

fluoridate water using inexpensive adsorbents like paddy-husk carbon have failed to make any significant dent in the problem, recent studies in India have shown that the disease has acquired new serious dimensions. In parts of Andhra Pradesh where the disease has been known to be endemic, it was noticed that large numbers of adolescents and young adults had started to develop serious bone deformities generally characterized by marked genu-valgum (40, 41) manifestations that had never been seen in those areas in earlier years. The prevalence of these deformities ranged from about 2% in some areas to as high as 17% in others and was found to be higher in sorghum eaters than in those not subsisting on sorghum.

A series of studies revealed that this new aggravation of an ancient disease was related to the construction of the large Nagarjunasagar Dam, which had impounded large amounts of water. The sequence of events leading to these new manifestations was described as follows: Construction of dam and impounding of water → elevation of subsoil water in wide areas in the vicinity of the dam → soil alkalinity, changes in the concentration of trace elements in food grains grown in the area, and, in particular, an increase in concentration of molybdenum → increased urinary excretion of copper, osteoporosis (superadded to fluorosis) → genu-valgum. Positive evidence in support of this hypothesis has been forthcoming from several studies at the National Institute of Nutrition.

As a preventive measure, it was suggested that the rural poor should be advised against drawing water for drinking purposes from the wells in the area because of high fluoride concentrations. Instead the Government was advised that part of the impounded water, which was being diverted almost entirely for irrigation purposes through canals, should be made available for drinking purposes.

Here is an instance of an unexpected ecological repercussion of a developmental program that was envisaged as an unmixed blessing and would help irrigate vast tracts of land and grow more food.

LACTOSE INTOLERANCE

Chronic diarrhea arising as a result of intolerance to disaccharides owing to a deficiency of disaccharidases is now being reported from some parts of the world. The incidence of lactose intolerance is reported to be high among Asians and Africans and rare among Caucasians (5, 13, 14, 16). On the basis of these findings it was postulated that inclusion of milk in the diets of undernourished populations of developing countries might lead to undesirable sequelae such as abdominal discomfort and diarrhea.

Indian studies (50) showed that there was no correlation between signs of lactose intolerance, as determined by lactose-overloading tests, and the levels

of the enzyme. They pointed out that lactose intolerance demonstrated under the artificial conditions of the tolerance tests did not necessarily imply milk intolerance. Thus there was no reason to withhold milk from undernourished Asian children nor to provide them with lactase tablets every time they had a milk drink as was being suggested by some commercial interests. These observations helped to dispel doubts about a traditionally highly valued item of Indian diets.

OTHER CONTRIBUTIONS

The foregoing account does not do full justice to all the important recent Indian work in the field of human nutrition. The emphasis here has been only on studies related to major public health nutrition problems. Significant contributions to nutrition science such as those of Ganguly (17) on vitamin A metabolism, of Bamji et al (3, 4) on riboflavin nutrition, and of Bhavani Belavady (6–9) and Gopalan (18–20, 29) on aspects of human lactation, to mention only a few, have not been discussed.

Perhaps the most important contributions, although the least spectacular, are the continuing investigations, compilations, and updating of information on the nutritive value of Indian foods (31)—the work that provides the basic foundation for all dietary recommendations and programs for dietary improvement. However, as mentioned at the outset, I have sought not to present a comprehensive catalogue but rather to give a few select examples of Indian scientific contributions to the amelioration of undernutrition in developing countries.

SUMMARY

Since diseases directly related to undernutrition are the major public health problems of India, nutrition research in the country has been largely directed towards elucidating their causes and identifying the most feasible methods for their prevention and control. This effort is an interdisciplinary exercise carried out in the laboratory, the clinic, and the field, with close interaction among biochemists, clinicians, and epidemiologists. Some of the identified solutions have found practical application; but, as in other areas of scientific endeavor, a gap exists between the acquisition of knowledge in the laboratories and its application in the field. Today, thanks to research efforts of the last few decades, we have the knowledge with which most diseases related to undernutrition can be prevented. Unfortunately, however, we do not always have the means of applying this knowledge under real-life conditions in the field. Even so, nutrition research during the last few decades has contributed significantly to the amelioration of undernutrition among poor communities in India.

Literature Cited

1. Adiga, P. R., Rao, S. L. N., Sharma, P. S. 1963. Some structural features and neurotoxic action of a compound from *L. sativus* seeds. *Curr. Sci.* 32:153
2. Agarwal, K. N., Agarwal, D. K., Srivastava, S. 1984. Emergence of goitre in Delhi. *Nutr. Found. India Bull.* 5(4):6–7
3. Bamji, M. S. 1969. Glutathione reductase activity in red blood cells and riboflavin nutritional status in humans. *Clin. Chem. Acta* 26:263–69
4. Bamji, M. S., Bhaskaram, P., Jacob, C. M. 1987. Urinary riboflavin excretion and erythrocyte glutathione reductase activity in preschool children suffering from upper respiratory infections and measles. *Ann. Nutr. Metab.* 31:191–96
5. Bayless, T. M., Rosenweig, N. S. 1966. A racial difference in incidence of lactase deficiency. A survey of milk intolerance and lactase deficiency in healthy adult males. *J. Am. Med. Assoc.* 197(12):968–72
6. Belavady, B. 1969. Nutrition in pregnancy and lactation. *Indian J. Med. Res.* 57:63–74
7. Belavady, B. 1980. Dietary supplementation and improvement in lactation performance of Indian women. In *Maternal Nutrition During Pregnancy and Lactation,* ed. H. Aebi, R. Whitehead, pp. 264–73. Bern: Hans Huber
8. Belavady, B., Gopalan, C. 1959. Chemical composition of human milk in poor Indian women. *Indian J. Med. Res.* 47:234-45
9. Belavady, B., Gopalan, C. 1960. Effect of dietary supplementation on the composition of breast milk. *Indian J. Med. Res.* 48:518–23
10. Belavady, B., Gopalan, C. 1965. Production of black tongue in dogs by feeding diets containing jowar (Sorghum vulgare). *Lancet* 2(424):1220–21
11. Belavady, B. L., Srikantia, S. G., Gopalan, C. 1963. The effect of the oral administration of leucine on the metabolism of tryptophan. *Biochem. J.* 87:652–55
12. Bender, D. A. 1983. Effects of a dietary excess of leucine on the metabolism of tryptophan in the rats: a mechanism for the pellagragenic action of leucine. *Br. J. Nutr.* 50:25–32
13. Bolin, T. D., Davis, A. E. 1969. Asian lactose intolerance and its relation to intake of lactose. *Nature* 222:382–83
14. Cook, G. C., Kajubi, S. K. 1966. Tribal incidence of lactose deficiency in Uganda. *Lancet* 1(440):725–29
15. Desikachar, H. S. R. 1981. Malting as an aid in reduction of viscosity of cereal and legume based diets. *Nutr. Found. India Bull.,* April, p. 6
16. Flatz, G., Saengudom, C., Sanguanbhokhai, T. 1969. Lactose intolerance in Thailand. *Nature* 221:758–59
17. Ganguly, J. 1989. *Biochemistry of Vitamin A*. Boca Raton, Fla: CRC Press. 221 pp.
18. Gopalan, C. 1956. Protein intake of breastfed poor Indian infants. *J. Trop. Pediatr.* 2:89–92
19. Gopalan, C. 1958. Studies on lactation in poor Indian communities. *J. Trop. Pediatr.* 4:87–97
20. Gopalan, C. 1962. Effect of nutrition on pregnancy and lactation. *Bull. WHO* 26:203–11
21. Gopalan, C. 1968. Kwashiorkor and marasmus. Evolution and distinguishing features. In *Calorie Deficiencies and Protein Deficiencies,* ed. R. A. McCance, E. M. Widdowson, pp. 49–58. London: Churchill
22. Gopalan, C. 1981. The National Goitre Control programme—a sad story. *Nutr. Found. India Bull.,* July, pp. 1–2
23. Gopalan, C. 1982. The nutrition policy of brinkmanship. *Nutr. Found. India Bull.,* October, pp. 5–6
24. Gopalan, C. 1983. Small is healthy? For the poor, not for the rich? *Nutr. Found. India Bull.,* October, pp. 1–5
25. Gopalan, C. 1984. Child survival and child nutrition. *Natl. Found. India Bull.* 5(1):1–3
26. Gopalan, C. 1984. The lathyrism problem—current status and new dimensions. *Sci. Rep. 2, Nutr. Found. India,* pp. 54–55
27. Gopalan, C. 1988. Stunting: Significance and implications for public health policy in linear growth retardation in less developed countries. *Nestle Nutrition Workshop Series, Nestec Ltd., New York,* ed. J. C. Waterlow, 14:266–69. Vevey: Raven
28. Gopalan, C. 1989. Undernutrition: measurement and implications. In *Nutrition, Health and National Development, Nutr. Found. India Spec. Publ. Ser.* 4:69–100
29. Gopalan, C., Belavady, B. 1961. Nutrition and lactation. *Fed. Proc.* 20(Suppl. 7):177–84
30. Gopalan, C., Narasinga Rao, B. S. 1971. Nutritional constraints on growth and development in current Indian dietaries. *Proc. Nutr. Soc. India* 10:111
31. Gopalan, C., Rama Sastri, B. V., Balasubramanian, S. C. 1971. *Nutritive Value of Indian Foods*. Revised and updated by B. S. Narasinga Rao, Y. G.

Deosthale, K. C. Pant. 1989. Hyderabad: Natl. Inst. Nutr., Indian Counc. Med. Res. 156 pp.
32. Gopalan, C., Srikantia, S. G. 1960. Leucine and pellagra. *Lancet* 1:954–57
33. Gopalan, C., Swaminathan, M. C., Krishnakumari, V. K., Rao, D. H., Vijayaraghavan, K. 1973. Effect of calorie supplementation on growth of undernourished children. *Am. J. Clin. Nutr.* 26:563–566
34. Gopaldas, T., Mehta, D., Chinnama, J. 1988. Reducing the bulk of cereal weaning gruels—a simple technology for rural homes. *Natl. Found. India Bull.* 9(1):5–8
35. Jaya Rao, K. S. 1974. Evolution of kwashiorkor and marasmus. *Lancet* 1(860):709–11
36. Jaya Rao, K. S., Srikantia, S. G., Gopalan, C. 1968. Plasma cortisol levels in protein calorie malnutrition. *Arch. Dis. Child.* 43:365
37. Kochupillai, N. 1984. Neonatal thyroid status in iodine deficient environment of sub Himalayas region. *Indian J. Med. Res.* 80:293–99
38. Kochupillai, N., Godbole, N. M. 1986. Iodised oil injections in goitre prophylaxis: possible impact on the newborn. *Nutr. Found. India Bull.* 7(4): 1–3
39. Kochupillai, N., Yalow, R. S. 1978. Preparation, purification and stability of high specific activity I 125-labelled thyronines. *Endocrinology* 102(1):128–35
40. Krishnamachari, K. A. V. R., Krishnaswamy, K. 1973. Genu valgum and osteoporosis in an area of endemic fluorosis. *Lancet* 2(834):877–79
41. Krishnamachari, K. A. V. R., Krishnaswamy, K. 1974. An epidemiological study of the syndrome of genu valgum among residents of endemic areas for fluorosis in Andhra Pradesh. *Indian J. Med. Res.* 62:1415
42. Krishnaswamy, K. 1979. Role of pyridoxine in pellagra—V. N. Patwardhan Prize Oration, *Indian Counc. Med. Res. Bull.* 9(1):1–3
43. Krishnaswamy, K., Rao, S. B., Raghuram, T. C., Srikantia, S. G. 1976. *Am. J. Clin. Nutr.* 29:177–81
44. Magboul, B. I., Bender, D. A. 1983. The effect of dietary excess of leucine on the synthesis of nicotinamide nucleotides in the rat. *Br. J. Nutr.* 49:321–29
45. Mohan, V. S., Nagarajan, V., Gopalan, C. 1966. Simple practical procedure for the removal of toxic factors in *L. Sativus*. *Indian J. Med. Res.* 54:410
46. Nagarajan, V., Roy, D. N., Mohan, V. S., Gopalan, C. 1963. *Ann. Rep., Nutr. Res. Lab., Indian Counc. Med. Res., Hyderabad,* pp. 39–40
47. Narasinga Rao, B. S. 1981. Control of anaemia by fortification of common salt with iron. *Nutr. Found. India Bull.,* April, pp. 7–8
48. Raghuramulu, N., Srikantia, S. G., Narasinga Rao, B. S., Gopalan, C. 1965. Nicotinamide nucleotides in the erythrocytes of patients suffering from pellagra. *Biochem. J.* 96:837–39
49. Reddy, V., Mohanram, M. 1971. Urinary excretion of lysosomal enzymes in hypovitaminosis and hypervitaminosis A in children. *Int. J. Vitam. Nutr. Res.* 41:321–26
50. Reddy, V., Pershad, J. 1972. Lactose intolerance in Indians. *Am. J. Clin. Nutr.* 25:114
51. Reddy, V., Sivakumar, B. 1972. Studies on vitamin A absorption. *Indian Pediatr.* 9:307–10
52. Reddy, V., Srikantia, S. G. 1966. Serum vitamin A in kwashiorkor. *Am. J. Clin. Nutr.* 18:34–37
53. Report of the Working Group on Fortification of Salt with Iron. 1972. *Am. J. Clin. Nutr.* 35:1442–51
54. Roy, D. N., Nagarajan, V., Gopalan, C. 1963. Production of neurolathyrism in chicks by the injection of *Lathyrus sativus* concentrates. *Curr. Sci.* 32:116–18
55. Satyanarayana, K. 1989. Body mass index, nutritional status and productivity. *Nestle Found., Lausanne, Ann. Rep.*
56. Satyanaranayana, K., Naidu, A. N., Chatterjee, B., Rao, B. S. N. 1977. Body size and work output. *Am. J. Clin. Nutr.* 30:322–25
57. Satyanarayana, K., Naidu, A. N., Rao, B. S. N. 1979. Nutritional deprivation in childhood and the body size, activity and physical work capacity of young boys. *Am. J. Clin. Nutr.* 32:1769–75
58. Satyanarayana, K., Venkataramana, Y., Someswara Rao, M. 1989. Nutrition and work performance: studies carried out in India. *Proc. Int. Congr. Nutr., 14th, Seoul,* 1:302–5
59. Shetty, P. S. 1990. Energy metabolism in chronic energy deficiency. Dr. S. G. Srikantia memorial lecture. *Proc. Nutr. Soc. India* 36:89–98
60. Short, H. M., McRobert, G. R., Bernard, T. W., Nayar, A. S. M. 1937. Endemic fluorosis in Madras Presidency. *Indian Med. Gaz.* 72:369–98
61. Singh, A., Jolly, S. S. 1961. Endemic fluorosis. *Q. J. Med.* 30:357
62. Srikantia, S. G. 1969. Protein calorie

malnutrition in Indian children. *Indian J. Med. Res.* 57(8):36–53 (Suppl.)
63. Swaminathan, M. C. 1971. Prevention of vitamin A deficiency by administration of massive doses of vitamin A. *Proc. Asian Congr. Nutr., 1st, Hyderabad,* pp. 696–701
64. Swaminathan, M. C., Susheela, T. P., Thimmayamma, B. V. S. 1970. Field prophylactic trial with a single annual oral massive dose of vitamin A. *Am. J. Clin. Nutr.* 23:119–22
65. Vijayaraghavan, K., Naidu, A. N., Rao, N. P., Srikantia, S. G. 1975. A simple method to evaluate the massive dose vitamin A prophylaxis programme in pre-school children. *Am. J. Clin. Nutr.* 28(10):1189–93