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COMBATING MALNUTRITION—PRACTICAL LEADS FROM SCIENTIFIC RESEARCH IN INDIA*

C GOPALAN, FNA

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

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The term ‘malnutrition’, in this presentation, is being used in a restricted sense to refer to major health disorders in the country associated with undernutrition and poverty. We are not discussing here the disorders of the affluent generally associated with ‘malnutrition’ of a different kind—namely ‘overnutrition’, though these are not unimportant. Undernutrition, however, is today the single most important factor undermining health, productivity and quality of our Human Resources and must, therefore, command immediate major concern and highest priority. Undernutrition and the state of illhealth associated with it arise not just from dietary deficiency alone but from the synergistic interaction of poor dietaries and poor environmental hygiene—the two major attributes of the pervasive “poverty syndrome”.

It is, no doubt, true that, in the ultimate analysis, the eradication of undernutrition can only be achieved through socioeconomic development and elimination of poverty. But this consideration should in no way obscure the overriding need for scientific research in Human Nutrition and the important practical contributions that such research can offer. In India, as in all poor developing countries, there is a whole spectrum of specific nutritional deficiency diseases, the precise pathogenesis and approach to prevention of each of which needs careful elucidation. In situations, like those obtaining in most developing countries, where undernutrition is widespread and resources to combat it are scarce, scientific research in nutrition acquires special relevance and importance and can help to identify feasible and cost-effective strategies for prevention and control. Health disorders associated with affluence and overnutrition, like obesity and atherosclerosis, for example, mostly afflict populations of prosperous developed countries and, therefore, naturally receive major attention and research support in those countries. On the other hand, scientific research on diseases of undernutrition must necessarily have to find top priority in the scientific agenda of poor developing countries. Undernutrition is our problem, not theirs. However, this is not to deny that outstanding basic contributions to nutrition science, which have benefited mankind in general

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(including developing and developed countries) have emerged from research in
developed countries.

The major point that will be made in this presentation is that scientific
research in India on problems of undernutrition during the last three decades has
in fact helped to generate several practical leads for action. It may be legitimately
claimed that some of these contributions have been pioneering and have helped
to enrich Nutrition Science in general. The sad fact that the several practical
leads thus generated through painstaking research, have not always been put to
optimal use because of inadequacies in our Health and Rural Development systems
cannot detract from their inherent scientific merit and practical value. Some
examples of practical leads that had emerged from scientific research in Human
Nutrition in the country in recent years are briefly discussed below. What
follows is by no means a comprehensive catalogue of notable nutrition research
contributions from India but only selected examples of contributions which have a
direct bearing on major nutritional diseases encountered in the country today.

MAJOR NUTRITIONAL PROBLEMS

The most outstanding nutritional problems in the country which, today, account
for significant impairment of the quality of the country’s Human Resources are:
Protein energy malnutrition (PEM) leading to physical and mental retardation and
underdevelopment of several thousands of children; vitamin A deficiency leading
to keratomalacia and nutritional blindness; widespread iron-deficiency anaemia
impairing the productivity and increasing the vulnerability of poor populations to
infections; and endemic goitre and other iodine-deficiency manifestations affecting
physical growth and mental development. With respect to each of these problems,
nutrition research in India has made important original contributions.

Other nutritional problems of the country which are somewhat more limited
in distribution, but which, nevertheless, present fascinating challenges to the
biologist and health scientists are: pellagra, in the Deccan plateau; fluorosis in
some parts of India, lathyrisim in Central India and ‘lactose intolerance’. Indian
scientific contributions towards the elucidation of the pathogenesis and prevention
of these problems also have been no less impressive.

PROTEIN-ENERGY MALNUTRITION (PEM)

PEM has, as it were, held the central stage in global nutrition research for now
nearly three decades. There have been numerous publications on this subject
from India, but for our present purpose we may highlight two important Indian
contributions which had helped to bring about a major change in prevailing
perceptions regarding its pathogenesis and approach to its prevention.

The first was the clear demonstration that the primary dietary deficiency
underlying PEM in India was not that of protein (as was hitherto being widely
claimed) but that of calories. Careful surveys of dietaries of under-fives in
different parts of the country among communities in whom PEM was common,
showed that while the daily protein intake ranged from 2.8 g/kg body weight to 1.7 g/kg—levels, which on the basis of widely accepted international and national recommendations, could be considered adequate, the daily calorie intakes were of the order of 70 to 75 kcal/kg as against the figure of 100 kcal/kg generally considered adequate. While the diets of over 90 per cent of children were deficient in calories, only those of 35 per cent were deficient in protein; even with regard to these latter children, if food intake had been raised to meet their calorie requirement, the protein needs would have been met. There was practically no situation when the children's diets were adequate with regard to calories but deficient with regard to protein alone.\textsuperscript{12}

That in the prevailing dietary of children of poor communities it was the calorie gap that was crucial was further demonstrated in yet another longitudinal study (of 14 months)\textsuperscript{13} of a community of poor children whose daily diets provided no more than 700 kcal (with 18 g protein daily). In this study it was shown that when the calorie gap in these diets was bridged through the supplementation of 300 additional kcal daily, derived from carbohydrate and fat sources (wheat flour, sugar and edible oil) with little additional protein—no more than 3 gms—("empty calories") growth performance could be significantly improved and clinical manifestation of PEM could be 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 have to depend on imports of expensive protein-rich concentrates (fish-protein concentrates were in fact sought to be widely promoted by several commercial interests), but can 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.

It may be pertinent to point out that the foregoing views on the PEM problem, based on research in India, were presented more than 20 years ago at a time when the "protein lobby" was riding high and any suggestion that it was the 'calorie gap' rather than 'protein gap' that was crucial, could be treated as heresy. In retrospect, it will be seen that Indian research contributions, despite the resistance they had initially roused in international circles (Protein—advisory group—PAG) eventually found wide acceptance as evidenced by the great "protein fiasco" and the closure of PAG following thereon. It must be added that Indian scientific contributions which sought to put the PEM problem in proper focus, had found influential scientific support both in developing and developed countries outside India even at the height of the "protein controversy".

**THE PRACTICAL CHALLENGE**

The real challenge in the prevention of PEM then boils down to ensuring that children under 5 years of age (especially under 3 years) get their habitual cereal-legume-vegetable foods in amounts adequate to meet their calorie needs—which unfortunately is not the case even at present. The prevailing calorie gap of about
300 k. calories daily in the dietaries of under-fives of poor communities in the country can be bridged with a fraction of the buffer-stocks of foodgrains that we now hold; and yet in the prevailing socio-economic order we are witness to the sad paradox of vast buffer stocks of foodgrains posing storage problems on the one hand, and vast sections of the poor unable to get the food they badly need on the other. Nutrition research has at least helped to expose the stark reality of such inequalities in our present national scene.

Yet another 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.9

We may now proceed to consider the second major contribution to the understanding of the PEM problem. It is well recognised that there are two distinct clinical syndromes associated with PEM—namely kwashiorkor and marasmus. (Marasmus in early infancy associated with highly inadequate intakes of milk—"infantile marasmus" has to be considered as a separate category. We are here considering marasmus in the pre-school child). At any given point of time (point-prevalence), it may be computed on the basis of available survey data that while roughly about 1 per cent of under-threes in poor communities may exhibit kwashiorkor, nearly 2 per cent to 3 per cent may show marasmus. Thus, at any point of time, among our poor communities we may expect to see several thousands of poor children suffering from kwashiorkor and several thousands more suffering from marasmus, both of them 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—the former due primarily to "protein deficiency and calorie excess" and the latter due to calorie deficiency. If this was really the case we would have had on our hands two major public health problems requiring two entirely different approaches to their prevention and control. Our studies lead us to the conclusion that this is fortunately not the case.

A major contribution of immense practical significance has been the clarification 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. The differences in the clinical and biochemical features of kwashiorkor and marasmus have been set out in Table I.

On the basis of intensive studies of the actual dietaries of children suffering from these two syndromes and of their hormonal profile, we had postulated that
Table I

Kwashiorkor and Marasmus (distinguishing features)

<table>
<thead>
<tr>
<th></th>
<th>Marasmus</th>
<th>Kwashiorkor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emaciation</td>
<td>++ +</td>
<td>+</td>
</tr>
<tr>
<td>Oedema</td>
<td>-----</td>
<td>++</td>
</tr>
<tr>
<td>Fatty infiltration of liver</td>
<td>-----</td>
<td>++</td>
</tr>
<tr>
<td>Serum albumin</td>
<td>Almost Normal</td>
<td>Markedly lowered</td>
</tr>
<tr>
<td>Serum enzymes:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lipase</td>
<td>Normal</td>
<td>Markedly lowered</td>
</tr>
<tr>
<td>Amylase</td>
<td>Normal</td>
<td>Lowered</td>
</tr>
<tr>
<td>Esterase</td>
<td>Slightly lowered</td>
<td>Markedly lowered</td>
</tr>
<tr>
<td>Serum Cholesterol</td>
<td>Normal</td>
<td>Lowered</td>
</tr>
<tr>
<td>Response to epinephrine</td>
<td>Exaggerated</td>
<td>Lowered</td>
</tr>
<tr>
<td>Serum urea</td>
<td>Normal</td>
<td>Lowered</td>
</tr>
<tr>
<td>Serum Copper</td>
<td>Normal</td>
<td>Lowered</td>
</tr>
<tr>
<td>Hair Copper</td>
<td>Normal</td>
<td>Lowered</td>
</tr>
<tr>
<td>Urinary urea/total urinary nitrogen</td>
<td>&gt; 65%</td>
<td>&lt; 50%</td>
</tr>
</tbody>
</table>

'Marasmus' represents the stage of attempted 'adaptation' to the nutritional stress wherein 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. Kwashiorkor represents the stage when this 'adaptation' breaks down. Further studies had 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 a breakdown of 'adaptation' at a later stage leading to kwashiorkor. 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 which 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 (Table II).

Table II

Hormonal profile in protein-calorie malnutrition

<table>
<thead>
<tr>
<th></th>
<th>Marasmus</th>
<th>Kwashiorkor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma Cortesol</td>
<td>Very high</td>
<td>High</td>
</tr>
<tr>
<td>Response to ACTH</td>
<td>Exaggerated</td>
<td>Normal or Poor</td>
</tr>
<tr>
<td>Plasma insulin</td>
<td>Normal</td>
<td>Normal or low</td>
</tr>
<tr>
<td>Response to stimuli</td>
<td>Normal</td>
<td>Impaired</td>
</tr>
<tr>
<td>Plasma High</td>
<td>Normal or low</td>
<td>High</td>
</tr>
<tr>
<td>Plasma Somatomedin</td>
<td>Normal</td>
<td>Low</td>
</tr>
<tr>
<td>Plasma PBI</td>
<td>Normal</td>
<td>Low</td>
</tr>
<tr>
<td>Plasma ADH</td>
<td>Normal</td>
<td>High</td>
</tr>
<tr>
<td>Urinary ADH</td>
<td>Normal</td>
<td>High</td>
</tr>
</tbody>
</table>

Source: NIN., Hyd., '74
These hormonal changes may help to ensure that in the face of stress posed by nutritional deprivation, muscle tissue is preferentially broken down in order 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 “contraction of the metabolic frontiers”. When adaptation eventually breaks down because of continued stress or of its aggravation by superadded factors like fresh infections etc., fatty infiltration of the liver, fall in serum albumin, reduction in serum enzymes and oedema ensure with the resultant picture of kwashiorkor. The fact that marasmus and kwashiorkor exist side by side in the same community subsisting on the same diets, as also the fact that marasmus and kwashiorkor could exist in the same child at different points of time lend support to the postulate that the two syndromes are but two facets of one and the same disease.

This clarification had helped to place the entire problem of marasmus and kwashiorkor in proper perspective as far as the public health approach to marasmus and kwashiorkor was concerned. We know that we are dealing with two manifestations of a single problem and that we do not need two divergent strategies for their control. It is hardly necessary to emphasise 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 fifties and sixties has been reviewed in an earlier publication.46

MISUSE OF THE TERM “ADAPTATION”

In the above discussion we have used the word ‘adaptation’ to refer to the organism’s response to stress. It is, however, important to emphasise that we are not using the term adaptation as being synonymous with normalcy and therefore as being something ‘acceptable’. Even a severely marasmic child with extreme emaciation but a normal liver is ‘adapted’! It is necessary to emphasise this in view of the loose manner in which the term ‘adaptation’ is now being misused to propagate the view that stunting and ‘moderate malnutrition’ in Third World children arising from PEM (which are not of such severity as to be life-threatening) may be viewed as acceptable ‘adaptation’, consistent with their culture (“cultural adaptation”) and environment (“Small is healthy”)?—For the poor not for the rich!). It is important in this connection to remind ourselves of the wise note of caution sounded by du Nony as quoted by Kamala S. Jaya Rao.25 “Adaptation is not progressive, but protective and defensive. When perfect adaptation is attained the organism makes no attempt at further transformation as long as the external stress continues. Therefore ... being adapted ......does not contribute to evolution. Adaptation is never a goal but only a means, a means to survival.”

It is perhaps not without significance that in keeping with the (implicit) suggestion that “moderate undernutrition” which is not life-threatening may be acceptable ‘adaptation’, the earlier goal of “child health” is being gradually
replaced by the slogan of "child-survival". In several recent publications\textsuperscript{15-16,17-18}, the author has 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.

*Keratomalacia and Nutritional Blindness*: The current global approach for the prevention of keratomalacia arising primarily from vitamin A deficiency, through the distribution of two massive annual oral doses of synthetic vitamin A—one each at six-monthly intervals—to children under 3 years of age, 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 gets released gradually to meet tissue needs had long been well-established. What was important, however, was (a) to establish the optimal dosage of vitamin A which while not being toxic will be adequate to afford protection to children against keratomalacia for fairly long durations; (b) to identify the most effective and feasible route and form of administration of the vitamin and (c) to demonstrate that under real-life conditions in the field, the administration of vitamin A in the dosage, frequency and form identified as above does help to 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 programme by the public-health agency. Through intensive work carried out in the clinic, laboratories and the field initiated by the National Institute of Nutrition nearly 25 years ago, it became possible for Indian scientists not only to develop this prophylaxis programme but to persuade the planners and policy-makers to incorporate this programme as an integral part of Primary Health Care operations in the country, in the Fourth Five Year Plan itself. The programme is now being continued, though it must be confessed that its implementation in some States of the country has not been effective—a reflection of the current inadequacies in our Health System. Other countries in the region such as Bangladesh, Nepal and Indonesia are also currently implementing a programme on more or less the same lines.

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

*Choice of Preparation*: In a preliminary trial in which a single dose of 300,000 IU of vitamin A given orally as a water-invisible preparation to a group of pre-school children, 25 per cent developed signs of acute though transient vitamin A toxicity characterised by raised intra-cranial tension (bulging fontanelles) restlessness and fever.\textsuperscript{47} When the same amount was given as an oil-soluble preparation, the incidence of toxic signs was 4 per cent. Moreover, animal studies had earlier shown that the best hepatic storage was achieved with oral administration of oil-soluble vitamin A.\textsuperscript{39} This decided the choice in favour of an oil-soluble preparation.
Route of Administration: Oral administration of 10000 IU of oily vitamin A produced significant increase in serum vitamin A levels but the same dose given intramuscularly had no such effect, as much of the vitamin continued to remain at the site of infection.\(^{39}\) Oral dosage was therefore preferred as also being more convenient to administer.

Optimal Dosage level for Sustained Effect: Longitudinal studies on groups of children showed that a single oral dose of 300000 IU was able to sustain normal levels of serum vitamin A in children for a period of 6 months. Studies in which 200000 IU of vitamin A was given along with labelled retinyl acetate, and urinary excretion of the label monitored, indicated that 70 per cent of the dose was absorbed and somewhat less than 50 per cent of the total dose was retained.\(^{40}\) That the administration of such a massive dose was not associated with significant lysosomal damage was demonstrated by the finding that there was either no increase or that an insignificant transient increase in the urinary excretion of lysosomal enzymes aryl sulphotase and acid phosphatase following the administration.\(^{41}\)

Field Trial: The real acid test of the efficacy of this prophylaxis approach consisted in the demonstration through a prolonged field trial extending to 5 years, including 2500 under-fives drawn from several villages, that with 300000 IU of vitamin A administered orally once a year and followed up for a period of 5 years, there was (a) a 75 per cent reduction in the overall incidence of vitamin A deficiency in the community and (b) that there was not a single new case of keratomalacia during this entire period and (c) serum vitamin A levels in children who received the dose were consistently higher than those who had not.\(^{48}\)

It was after all these extensive time-consuming tests had been completed that the scientists ventured to advise the Government of India to include this programme as part of routine Primary Health Care in at least 9 States of the Indian Union where there was evidence that vitamin A deficiency was more widely prevalent.

As a measure of abundant caution, in order to reduce risk of toxicity to the absolute minimum it was also recommended that the dose be reduced to 200,000 IU at a time and that it be given twice in the year—at six monthly intervals. A practical simple method, feasible under field conditions for the evaluation of the implementation of the programme was also developed.\(^{49}\)

All this may seem a success story. However, looking back on these efforts which were initiated a quarter of a century ago, and now looking at the results, we may legitimately ask whether all the expectations which prompted these efforts on the part of Indian nutrition scientists have in fact been fulfilled.

The control of nutritional blindness through the ‘short-cut’ of administration of synthetic vitamin A had been envisaged as a short-term approach—not as the permanent solution of the problem. It was always recognised that the ultimate solution lay in the promotion of the optimal use of B-carotene rich foods—green
leafy vegetables—in the diets of poor children. It must be confessed that the euphoria and complacence created by the introduction of the prophylaxis through massive dosage of synthetic vitamin A has to a considerable extent retarded research designed to develop and promote the better use of inexpensive B-carotene rich foods in the country. If such research has not altogether come to a standstill, it is proceeding, at best, at snail pace as an effort of low priority.

Secondly, the implementation of the prophylaxis programme is obviously tardy especially in States like Bihar. What is most disconcerting is that we do not have any authentic indication as to what real impact the prophylaxis programme has had on the nutritional blindness problem. The official figures of annual incidence 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 paediatric hospitals since the introduction of the programme. In the absence of such data, we are in no position to counter or confirm the claims that are frequently made.

It would seem that while on the one hand we are relying heavily on synthetic vitamin A administration as the answer to vitamin A deficiency which, as pointed out above, was not what was originally intended, on the other hand, we continue to be entirely dependent on a foreign commercial source for our supply of vitamin A concentrate. In short, we are veritably ‘at the mercy’ of foreign commercial interests with respect to a programme of such vital importance to national health. The claims that a major part of the vitamin A we need for our programmes is being ‘indigenously manufactured’ will again not stand scrutiny—unless we accept that ‘bottling’ and participation in the subsidiary and final stages of manufacture amounts to ‘indigenous manufacture’; the truth appears to be that the technical knowhow for the essential step in the manufacture of synthetic vitamin A rests with a foreign commercial source which virtually holds the monopoly in this regard. It is not clear as to why Indian scientists have shown no enthusiasm in achieving self-reliance in this regard and why no “Technology Mission” has been set up for this valid purpose.

While we may rejoice at our modest successes, we have still a long way to go. Recent research indicates that the implication of vitamin A deficiency may be more far-reaching than what we had earlier imagined. This is all the more reason that this subject should now receive renewed attention.

Iron Deficiency Anaemia: A major contribution of immense practical value has been the development of a technique for the fortification of common salt with iron. The research that was involved 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 anaemia 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 pre-school children and indeed even of adult men. A more recent study by the National Institute of Nutrition\textsuperscript{36} showed that 65 per cent of adult women, 75 per cent of pregnant women, 77 per cent of pre-school children and nearly 45 per cent of adult men in poor rural communities were anaemic. Anaemia is thus probably the most extensive nutritional deficiency disorder in the country. Recent research has indicated that apart from impairing productivity, the disease also carries quite a few other functional implications. Though Indian diets generally provide 20 to 30mg of iron daily, in view of their high phytate content because of the predominance of cereals, the bioavailability of dietary iron as determined by radioisotope technique is only 1 to 5 per cent.

The rational ultimate answer to the problem would, of course, consist in the diversification and improvement of the diets — a goal unlikely to be achieved in the near future. The programme of distribution of iron-folate tablets through 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 with iron. 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 real challenge here was to identify the formula for fortification which will satisfy the conflicting requirements of stability, acceptability and bioavailability. The formula which was identified as one satisfying these requirements by the National Institute of Nutrition consisted of ferro ortho phosphate (3.5g per kg) and sodium acid sulphate (5g per kg) as an absorption promoter, providing 1 mg iron per g of salt. Later this formula was further improved by the substitution of ferric phosphate by the much less expensive ferrous sulphate (3500 ppm) and orthophosphoric acid or sodium orthophosphate (2800ppm). With an estimated intake of 15gm of common salt per adult per day, common salt fortified as above will provide an additional 15mg 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 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\textsuperscript{36}. Following on this a multicentric study coordinated by the National Institute of Nutrition, 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 haemoglobin levels in the experimental and control group again helped to confirm the significant impact of the procedure on the anaemia problem (Report of the Working Group 1982). The Government of India have now been persuaded to undertake this programme at least in some parts of the country in the first instance.

An important hurdle that had to be crossed was to find if fortification of common salt with iron was compatible with the decision of the Government of
India to resort to universal iodation of common salt meant for human consumption in the country as a method of prevention and control of endemic goitre. Scientists of NIN have now been able to recently develop a feasible procedure for the simultaneous fortification of common salt with iron and iodine.

The above studies may perhaps lack the glamour of some ongoing research in ‘advanced’ areas of molecular biology and genetic engineering; but their merit consists in the fact that skills in the fields of organic chemistry, biochemistry, physiology and epidemiology were effectively combined and coordinated towards providing a practical solution to major health problems of the country.

Endemic Goitre and Iodine-Deficiency: According to some estimates more than 40 million people in the country suffer from goitre. The National Goitre Control Programme based on iodation of common salt which had been initiated in the later half of the fifties, after an initial promising start, had languished because of poor implementation and inept supervision. The emergence of new goitre-endemic areas has added fresh dimensions to the problem.

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

Parenteral administration of iodised oil to pregnant women is now being promoted in some quarters as a suitable prophylactic approach in relatively inaccessible areas till such time as the salt iodation programme gathers full momentum. Recent Indian studies however, sound, a note of caution against resorting to this approach. According to these studies, iodised 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 iodised oils to pregnant mothers has been seriously questioned. These views have been challenged and there is apparently some controversy. It must, however, be clear that it will not be prudent to push ahead with any procedure regarding the safety of which serious doubts have been expressed, especially when a time-tested safe inexpensive alternative (salt iodation) is already available.

It is at least gratifying that thanks to our scientists, major decisions on technologies to be opted for in our national public health programmes are not
entirely dependent on advice and recommendations of foreign and international agencies.

The foregoing account deals with major nutritional deficiency disorders affecting vast numbers of the country's population. What follows is a brief account of scientific contributions from India towards the better understanding of four other nutritional disorders which, though 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 off a new series of studies on pellagra starting with a paper \(^{20}\) in which we had proposed that the high level of leucine in sorghum may play a positive role in the pathogenesis of the disease. The studies which followed showed that excess leucine in otherwise poor dietaries, could induce disturbances in the tryptophan—niacin pathway reflected in increased urinary excretion of quinolinic acid on leucine feeding \(^{5}\) decreased rate of synthesis of nicotinamid nucleotides by erythrocytes \(^{37}\) decreased activity of quinotinate phosphoribosyl transferase (QPRT) a key enzyme in NAD synthesis in livers \(^{4}\) and a fall in platelet 5-hydroxy tryptamine levels \(^{31}\).

From these studies it was concluded that excess leucine in poor sorghum diets could bring about significant changes in a number of key enzymes in the tryptophan—niacin pathway ultimately resulting in decreased nicotinamide nuleotide formation from dietary tryptophan—thus leading to conditioned deficiency of nicotinic acid.

In further studies it was shown that these effects of excess leucine could be countered by pyridoxin. Post-tryptophan load excretion of xanthurenic acid, kynurenic acid and quinolinic acid, which were initially raised in pellagrins were reduced after pyridoxin treatment \(^{32}\).

It would thus appear from the Indian studies that in the pathogenesis of pellagra (which is by no means exclusively confined to maize eaters only but which could also occur in sorghum eaters), apart from tryptophan deficiency (in maize eaters) leucine excess (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 USA. Some recent reports from England have, however, lent support to the observations from India. Magboul and Bender \(^{33}\) showed that diets which provide excess leucine brought
about "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 kynureninase." In a subsequent communication Bender reported that "dietary excess of leucine led to inhibition of kynureninase and increased the activity of piconilate carboxylase—which could be expected to explain decreased synthesis of nicotinamide nucleotides. The very fact that the Indian claims which started with a paper as early as 1960 and which, at one stage, were sought to be dismissed, still continue to attract attention, controversy and support is perhaps, by itself, of some significance.

**Lathyris**m: Neurolathyris characterised 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 when it was demonstrated that alcoholic extracts of lathyrus sativus could produce neurotoxic manifestations when injected into baby chicken. The toxic factor was subsequently isolated and identified as BOAA (B-oxalyl amino alanine). 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. Simultaneously attempts were also made by agricultural scientists in India to identify and selectively propagate genetic strains of lathyrus sativus low in BOAA but these attempts have not been successful; but are recently being revived in other parts of the world (Canada).

It must, however, be confessed that all the scientific research efforts that went in into the elucidation of the problem of lathyris have not directly resulted in the eradication of the disease. Attempts to ban the cultivation of the offending crop failed because the crop had the merit of being a hardy one that would grow on unirrigated land; it was the staple of the poor and there was no easy substitute. Recently, however, it would appear that following on 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. 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, it might have still done some good, 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 are active movements for fluoridation of water as a method for prevention of dental caries, in India, the problem in some parts of the country (especially Punjab and Andhra Pradesh) is the presence of excess fluoride in drinking water leading to skeletal changes which may sometimes be so severe as to be incapacitating.

Endemic fluorosis was in fact first identified in the country in some areas of the present Andhra Pradesh which were then parts of the erstwhile Madras Presidency. Subsequently, endemic fluorosis belts were also identified in Punjab. The disease affects the rural poor in areas where the drinking water may contain as high as 15 ppm of fluoride. While attempts to defluoridate water using inexpensive adsorbents like paddy-husk carbon have failed to make any significant dent on 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 started developing serious bone deformities generally characterised by marked genuvalgum manifestations which had never been seen in those areas in earlier years. The prevalence of these deformities ranged from about 2 per cent in some areas to as high as 17 per cent in others and was found to be higher in jowar eaters than those not subsisting on jower.

A series of interesting studies revealed that this new aggravation of this ancient disease was related to the construction of the large Nagarjunasagar Dam which had impounded large amounts of water. The sequence of events leading up to these new manifestations was 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 in the area and in particular increase in concentration of molybdenum in the foods grown—increased urinary excretion of copper—osteoporosis (superadded to fluorosis)—genu valgum. Positive evidence in favour of the actual occurrence of several steps briefly mentioned above has been forthcoming from the several studies at the National Institute of Nutrition.

As a preventive measure, in was suggested that the rural poor should be advised against drawing water for drinking purposes from the wells in the area—the water there being high in fluoride concentration. 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 programme’ which was envisaged as an unmixed blessing that would help to irrigate vast tracts of land and help grow more food.

Lactose Intolerance: Chronic diarrhoea arising as a result of intolerance to disaccharides due to 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. On the basis of
these findings it was being postulated that inclusion of milk in the diets of under-
nourished populations of developing countries may lead to undesirable sequelae 
such as abdominal discomfort and diarrhoea.

Indian studies\textsuperscript{38} showed that there was no correlation between signs of ‘lactose 
intolerance’ as determined by lactose overloading tests and the levels of the 
enzyme. It was pointed out that lactose intolerance demonstrated under the artifi-
cial conditions of the tolerance tests did not necessarily imply milk intolerance. It 
was thus shown that there was no case for withholding milk from undernourished 
Asian children, nor for providing them 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 dietaries.

I am deeply aware that the foregoing account does not do full justice to all 
the important recent Indian work in the field of Human Nutrition. For example, 
we have not discussed the basic contributions of the scientists of the Department 
of Biochemistry of the Indian Institute of Science and of the National Institute of 
Nutrition in the field of biochemistry of important vitamins; nor have we discussed 
the practical contributions of scientists of the Central Food Technological Research 
Institute (CFTRI) in the field of food technology, particularly with respect to the 
development of safe, feasible, though not glamorous, methods of food storage 
technology devoid of potential health hazards. The extensive work in India on human 
lactation, output and composition of breast-milk; on aflatoxicosis including 
the demonstration for the first time of the carcinogenic effect of aflatoxin in primates 
and the work on other food toxins; and the more recent work on the amount and 
nature of ‘invisible’ fat in cereals and pulses by Ghafoorunissa and Achaya which 
has provided new insights with respect to fat requirements in Indian dietaries, have 
not been mentioned. Perhaps the most important omission relates to what may 
be the least spectacular but probably the most useful continuing investigations and 
compilation of the nutritive value of Indian foods—the work which provides the 
basic data on which all our dietary recommendations rest. However, as I had 
pointed out even at the start, what has been attempted here is not a presentation 
of a comprehensive catalogue but of a few selected examples of Indian scientific 
contributions to the amelioration of undernutrition among our people.

\textit{Concluding Comments}: A complaint that is often voiced is that Indian scienti-
lists generally tend to pursue research on problems which are in current fashion in 
technologically advanced countries rather than on those which are of immediate 
relevance and practical importance to their own country. These latter problems 
may seem to lack ‘glamour’ and ‘visibility’ and may not offer promise of “international 
recognition”. They may not also call for ultra-sophisticated techniques—the 
use of which by itself is often mistakenly assumed to be a hallmark of distinc-
tion. Under the circumstances, it should not be surprising if the anxiety ‘keep in 
step’ with leaders “elsewhere” and to be considered as being in the mainstream of 
currently “hot” international scientific pursuits, often takes precedence over 
obvious national needs.
The foregoing account of Indian nutrition research contributions over the last few decades, however, will show that these criticisms will not apply at least to Indian scientists engaged in research in the field of Human Nutrition. Nutrition scientists have, by and large, tried to address the major problems right at their doorstep and the entire thrust of their research had been directed towards understanding the evolution of these problems and more importantly towards identifying practical solutions to them—solutions which can be applied given the present constraints. It must also be remembered that the overall budgetary allocation to nutrition research today represents a tiny fraction of the allocation to several other sectors which command highly articulate advocacy and visibility.

With respect to many areas of scientific activity there is a gap between the accumulation of knowledge in research laboratories and the practical application of that knowledge in the field for the good of the people. In no field of scientific activity is this gap perhaps greater (and more unfortunate and inexcusable) than in the field of Human Nutrition. Today we have the necessary technical knowledge gathered through painstaking research—and, to a great extent, also the resources—with which we can eliminate at least our major nutritional deficiency orders—even if we are in no position to ensure for our people a level of nutritional status comparable to those of advanced prosperous countries. But the implementation of practically every major nutrition programme—be it control of PEM, goitre, nutritional blindness, anaemia, lathyrism or fluorosis—is tardy and inefficient. A country which can join the race for exploration of space and expeditions to the Antarctic, which boasts of very impressive 'scientific manpower' and is "among the top ten" industrial powers of the world, apparently finds itself unable to summon necessary political will and administrative competence to wipe out diseases which needlessly afflict millions of her people—diseases which have long ago been eliminated from the rest of the civilised world and for the elimination of which the scientific know-how and requisite material and manpower resources are available within the country.

It is not that we scientists have all the answers; nor is it that our answers are all necessarily sound and feasible. Our accomplishments do not merit wild jubilation but justify some optimism. There is undoubtedly considerable scope and need for continued maintenance, and indeed further improvement, of the quality and range of nutrition research in the country. There is absolutely no room for complacency; the unfinished tasks that lie ahead are truly formidable. While practically all the 'old' problems of undernutrition are still very much with us, 'new' problems are emerging. The 'successful' green revolution has unleashed a major deterrent repercussion—namely the progressive reduction in per caput availability of pulses (legumes), the poor man's protein. There is reason to believe that for this reason, the quality of the dietaries in our poorest households has actually deteriorated sharply during recent years: in the wake of intensive agricultural technology ill-mentioned changes in soil chemistry have been induced and these may be expected to be reflected in distortions of trace element composition of foods; new goitre-endemic areas are being identified; with the demographic
transition nutritional problems of the aged are coming to the fore; with increasing urbanisation, nutritional problems of urban slums are gathering in intensity. Since our current health programmes largely stop with "death-control strategies" ('child survival' and 'oral rehydration'), we may expect that marginal reductions in child mortality will be accompanied by increasing prevalence of childhood malnutrition in the next two decades. At the other end of the socio-economic spectrum we may also expect increasing incidence of degenerative diseases brought on by increasing life expectancy and overnutrition associated with affluence. All this is not to paint a pessimistic picture of the future but merely to forewarn that the challenges which the nutrition scientists may face in the next two decades may prove even more formidable and exacting than those of the last three decades. For this reason, Nutrition Research must receive much higher priority and support in our national scientific agenda in the future than in the past.

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