In this paper we briefly review some of our recent work on the nutritional aspects of leprosy, and also draw attention to related contributions of other scientists in India and abroad.

Foster et al. had recently reviewed the available literature on nutrition-leprosy inter-relationship (145 references). Despite much suggestive evidence of the supportive contributory role of good nutrition towards better prognosis and management of leprosy, the precise role of specific nutrients in the pathogenesis of leprosy is still not clear. This is an area — hitherto somewhat neglected — which merits serious attention from nutrition scientists and leprologists. We hope that this brief report will stimulate further interest in this area.

Protein-Energy Nutrition in Leprosy

Rao et al. measured body-mass indices of lepromatous patients and compared the data with those of age and sex-matched controls in the mining district of Singhbhum in Eastern India. They also estimated the daily protein and energy intakes of the two groups using weightment and oral questionnaire methods.

Fifty-two percent of lepromatous subjects and 39 percent of control subjects, both belonging to poor income groups, could be considered as being in grade II undernutrition on the basis of their anthropometric status. While 13 percent of the patients could be classified as falling under grade I undernutrition on the basis of their anthropometric status, there were 14 percent controls in this category. There was no subject (cases or controls) suffering from grade III undernutrition. These data would show that nearly one-third of lepromatous cases did not show anthropometric evidence of undernutrition. Differences in the calorie intake of cases and controls were marginal and apparently not significant. These data, despite their limitations, would seem to provide no evidence of the contributory role of protein-energy undernutrition in leprosy.

Table 1: Vitamins A and E levels in normal controls and leprosy patients (Mean ± S.D.)

<table>
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<tr>
<th>Group</th>
<th>vitamin A (µg/dl)</th>
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<tr>
<td>Normal controls</td>
<td>24.09 ± 7.57*</td>
<td>0.69 ± 0.22*</td>
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<td>Leprosy patients</td>
<td>12.06 ± 2.14</td>
<td>0.41 ± 0.04</td>
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<tr>
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<td>0.36 ± 0.22</td>
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<tr>
<td>BL</td>
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<td>0.37 ± 0.16</td>
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<tr>
<td>BB</td>
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<td>BT</td>
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<tr>
<td>Histoid</td>
<td>10.3 ± 4.03</td>
<td>0.407 ± 0.25</td>
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Statistical analysis was done by students 't' test.

Vitamin Deficiency

B vitamins: While Muir had reported in 1928 that deficiency of vitamin B complex did not aggravate the severity of the disease, Badger and Sebrell had claimed, on the basis of studies on experimental animals, that thiamine deficiency resulted in generalised infection and shorter incubation period. In a recent study, Saha and Rao found no significant differences in serum folate and serum vitamin B levels as between lepromatous subjects and controls.

Fat-soluble vitamins: Rao et al. observed a moderate lowering of serum vitamin A levels in tuberculosis leprosy patients and a more marked reduction in lepromatous subjects (Table 1) — an observation in line with the earlier report of Sher et al. of a significant lowering of serum vitamin A levels in lepromatous leprosy patients in comparison with tuberculosis leprosy cases. In fact, Sher et al. and later Rao and Saha had shown that as the pathological spectrum of leprosy shifted from the tuberculoid to the lepromatous end, there was a progressive fall in serum vitamin A levels.

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Statistical analysis was done by students 't' test.

*LL, BL, BB, BT, Histoid vs. controls, p < 0.001, Highly significant.
Rao et al. had also reported that serum vitamin A transport proteins, such as pre-albumin and retinol binding protein (RBP) levels were low in lepromatous patients as compared to healthy controls (Table 2). Bharadwaj et al. had reported low levels of vitamin A in the serum and skin of leprosy patients under clofazimine treatment.

Saha and Rao had reported comparable serum concentrations of 25-hydroxy vitamin D levels in lepromatous leprosy patients and normal subjects. Rao and Saha had also found that serum concentrations of vitamin E (like those of vitamin A) showed a gradual progressive reduction over the entire leprosy spectrum as compared to values in control subjects (Table 1).

The reduction in serum levels of vitamin A and E observed in leprosy subjects seemed to be disease-related; because as the disease advanced from the immunocompetent tuberculoid state to the immunocompromised lepromatous stage, the serum concentration of the two vitamins progressively declined.

It is interesting in this connection that as early as 1921, Rogers in Calcutta had claimed that administration of cod liver oil to leprosy patients caused some regression of leprosy lesions.

It is necessary that the significance of the changes in the serum vitamin A and E levels in the different clinical forms and stages of leprosy is further elucidated through well-controlled studies on suitable experimental models and the effects of vitamin A and E supplementation on the course of the disease and on the response to therapy in established cases, carefully assessed.

As early as 1955, Manson and Bergel had reported that in rats and hamsters fed on a vitamin E deficient diet, rich in unsaturated fatty acids, growth of M. leprae was promoted. Bergel proposed that "an altered metabolic ecosystem" increased lipid autooxidation which in turn made the "ground suitable" for multiplication of M. leprae. These observations need to be placed on firmer and more precise footing. Clearly, there are still many gaps in our understanding of the possible role of the fat soluble vitamins A and E in the pathogenesis and evolution of leprosy.

**Trace elements:** Perhaps, apart from the changes reported above with respect to serum vitamin A and vitamin E levels, the most consistent findings are those related to serum zinc and copper levels in leprosy.

Significantly low serum zinc levels and hypercupraemia in the case of leprosy have been reported by a number of authors, Venkatesan et al., Sher et al., Mathur et al. and Rao et al. A faster subsidence of erythema nodosum leporosum has also been reported by some of the same authors following the administration of zinc. The significance of hypozincemia and hypercupraemia and the biochemical mechanisms underlying these phenomena need to be elucidated through further studies.

A reverse relationship between serum zinc and serum copper levels has been well-recognized. That the change in zinc and copper in leprosy is disease-related and not diet-related was shown by Rao and Saha, who found that there were no striking significant differences between cases of leprosy and controls with respect to dietary intake of zinc and copper (Table 3). Also cases of leprosy from higher income groups with a better dietary intake of zinc showed the same order of hypozincemia as those of the poorer income groups and lower dietary zinc intake.

Rao et al. also found that the serum levels of "diet-independent" proteins such as Ig G (2075 ± 592 mg/dl) were not reduced in the leprosy patients in relation to normal controls (1545 ± 419 mg/dl), while those of "diet-dependent" proteins such as serum albumin, RBP and prealbumin were decreased in lepromatous patients in comparison to the controls (Table 2). Hypozincemia might be responsible for the hypoaalbuminaemia. Alternatively low serum albumin levels may be attributable to the binding of serum albumin with dapsone. Lowered serum concentration of prealbumin and RBP might also be related to the lowered serum zinc levels; positive correlations between serum vitamin A levels and zinc levels were observed in lepromatous leprosy patients.

**Serum iron:** Sher et al. had reported significant lowering of serum iron in lepromatous patients (50.1 mg/dl) as compared to tuberculoid patients (99.3 mg/dl), but serum transferrin levels in the two groups were similar. On the other hand, Rao et al. found that serum levels in lepromatous subjects (153 mg/dl) and in normal controls (152 mg/dl)

---

**Table 2:** Serum levels of zinc binding protein (albumin and macroglobulin) and vitamin A binding protein (retinol binding protein and prealbumin) in controls and lepromatous patients

<table>
<thead>
<tr>
<th>Group</th>
<th>Albumin g/100 ml</th>
<th>Alpha-2-macroglobulin mg/100 ml</th>
<th>RBP mg/100 ml</th>
<th>Prealbumin</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n)</td>
<td>(n)</td>
<td>(n)</td>
<td>(n)</td>
</tr>
<tr>
<td>Controls</td>
<td>4.4</td>
<td>313</td>
<td>3.09</td>
<td>22</td>
</tr>
<tr>
<td></td>
<td>(36)</td>
<td>(38)</td>
<td>(26)</td>
<td>(32)</td>
</tr>
<tr>
<td>Lepromatous</td>
<td>3.9</td>
<td>308</td>
<td>2.56</td>
<td>11</td>
</tr>
<tr>
<td>leprosy patients</td>
<td>(36)</td>
<td>(35)</td>
<td>(68)</td>
<td>(56)</td>
</tr>
</tbody>
</table>

Except alpha-2-macroglobulin, serum albumin, RBP and prealbumin levels were low in the patient group.

**Table 3:** Association of per capita income with dietary intake and serum levels of zinc and copper in healthy subjects and leprosy patients

<table>
<thead>
<tr>
<th>Group</th>
<th>Per capita income less than Rs.150</th>
<th>Per capita income more than Rs.150</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Zinc</td>
<td>Copper</td>
</tr>
<tr>
<td>a) Healthy subjects</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dietary intake (g/day)</td>
<td>5.22</td>
<td>1.32</td>
</tr>
<tr>
<td>Serum levels (µg/dl)</td>
<td>113</td>
<td>99</td>
</tr>
<tr>
<td>b) Lepromatous patients</td>
<td>5.7</td>
<td>1.27</td>
</tr>
<tr>
<td>Serum level (µg/dl)</td>
<td>69.9</td>
<td>205</td>
</tr>
</tbody>
</table>

Daily recommended intake of zinc and copper are 12.0 mg and 2.50 mg respectively.
were nearly similar and so were the serum transferrin levels. Rao et al\textsuperscript{10} also found that serum ferritin levels in lepromatous males (120.8 mg/dl) and females (54.8 mg/dl) were comparable to the values observed in normal controls (96.7 mg/dl in males and 43 mg/dl in females respectively). However, Rao et al\textsuperscript{10} noted significant reduction in haemoglobin levels in lepromatous patients as compared to normal subjects. Again the significance of these observations needs to be investigated.

**Nutrition And Metabolism Of Anti-leprosy Drugs**

Although there are many studies on the adverse effects of antileprosy drugs and although there are several reports on the modulation of the human immune system by the individual drugs, belonging to multi-drug therapy (MDT), i.e. dapsone, clofazidine and rifampicin there are few publications on the nutritional imbalance, if any, that might be produced by these drugs.

Krishnaswami\textsuperscript{6} at the National Institute of Nutrition, Hyderabad, had reported that in leprosy patients on dapsone therapy, the mean albumin and haemoglobin concentrations remained within normal limits. In an animal study, Saha\textsuperscript{17} (1990) had shown that rats fed on dapsone, clofazidine and rifampicin had shown a fall of W.B.C. count from 13990 ± 3797/ mm\(^3\) to 5396 ± 2241/ mm\(^3\) and a fall of haemoglobin level from 13.1 ± 0.64 g/dl to 11.3 ± 0.90 g/dl, but the dosages used in these studies were very large (human dosage levels) and the results may not be of practical significance.

Very little work has so far been done on the effect of antileprosy drugs on the metabolic enzymes handling drugs. In humans, prolonged administration of rifampicin is known to produce proliferation of hepatic smooth endoplasmic reticulum and enhanced content of cytochrome P-450, a drug metabolising enzyme, in isolated liver subfractions. Also hydroxylation of steroids, i.e. ethinyl estradiol and cortisol is found to be affected by rifampicin treatment.

Multi-drug therapy in leprosy is necessarily of prolonged duration. It is important that the impact of such therapy on the nutritional status of the subjects and on their nutrient requirements is clearly understood. It is also necessary to understand how such therapy may modify the patients' ability to mobilise other drugs that may be needed by them for other inter-current ailments.

The authors are from the Department of Immunology, Vallabhbhai Patel Chest Institute, New Delhi.

**References**


**REVIEWS AND COMMENTS**

**Nutrition And Leprosy**

The paper on Nutrition and Leprosy by Kunal Saha and Rao\textsuperscript{6} in the earlier pages should serve to draw attention to an important aspect of the problem of leprosy which must interest both nutrition scientists and leprologists.

It is estimated that the number of people suffering from leprosy in the world today may exceed 15 million. Of these, as many as 5 million live in India\textsuperscript{17}. There can be no doubt, therefore, that leprosy ranks as a major public health problem in our country today.

Hansen discovered the causative organism of leprosy - Mycobacterium Lepra, more than a century ago. The industrialised affluent countries of the world had successfully eradicated leprosy several decades ago - long before the modern powerful anti-leprosy drugs were even discovered. They achieved their success through strict segregation and all-round improvement in the living conditions of their people - including their health, sanitation and nutritional status, and not through specific control programmes based on drugs (which they did not have).

In India, the National Leprosy Eradication Programme was launched in 1954. As part of this programme, multi-drug therapy is being implemented in 85 leprosy-endemic districts of the country. Our present approach to the control of leprosy is, however, heavily (indeed almost entirely) drug-oriented. Apparently we are still far away from the goal of total eradication of the disease.

While we must undoubtedly pursue our present strategy of identifying cases of leprosy in the early stages and giving them the benefit of intensive multi-drug...
In order to prevent the occurrence of new cases, we must gain better insight into its epidemiology. There are some basic issues with respect to the epidemiology of the disease which have not, as yet, been adequately addressed. Out of the nearly 412 districts in the country, prevalence of leprosy, at a rate of five and above per thousand of population, has been observed in 212 districts - i.e. nearly half of the country. The other half of the country is relatively much less affected. Why is this so? The worst affected states are those of Tamil Nadu, Andhra Pradesh and Orissa (all in the South) where the prevalence rate exceeds 10 per thousand of population. On the other hand, in the states of Rajasthan, Haryana, Punjab, Himachal Pradesh (all in the North) and Assam and Arunachal Pradesh (in the East), the prevalence rate is less than two per thousand. The states of Gujarat, Madhya Pradesh, Uttar Pradesh and Kerala have a prevalence rate between two and four per thousand population. In general, therefore, the South (excluding Kerala) and the East (with the exception of Assam and Arunachal Pradesh) seem to bear the brunt, while the northern, central and western parts of the country are relatively much less affected. The three worst affected states together with West Bengal (prevalence rate of five to nine per thousand), all of which fall in the "rice belt", have also been traditionally the "hot-beds" of the most fulminating forms of undernutrition — beri beri, pellagra, nutritional blindness and kwashiorkor, and are still probably among the most poverty-stricken states in the country. Cases of leprosy include a sizeable proportion of children.

It may, however, not be justifiable to read too much into this association. While the co-existence of undernutrition and high prevalence of leprosy in some poor population groups may be suggestive of undernutrition-leprosy inter-relationship, it must be remembered that severe undernutrition has often been seen in poor population groups in the total absence of leprosy. There has been no evidence of exacerbation of leprosy-prevalence in leprosy-endemic areas in the wake of acute famine. Also, while a majority of cases of leprosy are poor and undernourished, the relatively affluent and well-nourished have not been totally exempt.

In a country like ours where both undernutrition and leprosy are widespread, and in the context of the availability of powerful drugs for the treatment of leprosy, it is necessary that studies on the nutrition-leprosy inter-relationship are intensified. Apart from the practical necessity for such studies, Indian scientists can make scientific contributions in this area which may not be possible in other locations.

There has not been much interest in the question of dietary management of leprosy cases. Considering the widespread prevalence of undernutrition and the fact that leprosy is a chronic ailment which calls for prolonged therapy, it is unfortunate that so little attention has been devoted to this aspect.

Saha and Rao's paper points to some consistent positive findings with respect to serum levels of vitamin A, vitamin E, zinc and copper in leprosy. The significance of these observations, from the point of view of susceptibility, pathogenesis and management of leprosy, needs to be clearly established through further intensive studies. In particular, it seems important to elucidate the possible relationship between leprosy and zinc nutrition.

The predominantly cereal-based dietaries of the poor in the country are not only low in zinc but the bioavailability of dietary zinc may also be expected to be low. Prasad, who had pioneered studies on zinc nutrition, had recently reviewed the spectrum of diseases that may be conditioned by zinc deficiency. Though he did not include leprosy in his masterly survey, it is interesting that in the Middle East, where Prasad had carried out his initial landmark studies on zinc, leprosy is also an important health problem. Can zinc nutritional status influence the acquirement, course, and progression of leprosy from the immunocompetent to the immunocompromised stage? Does zinc nutrition status condition the response to treatment? Rao and Saha found nearly the same order of hypozincaemia in cases of leprosy with varying levels of dietary intake of zinc, and concluded that hypozincaemia was a disease-related and not a diet-related phenomenon. This conclusion may not still rule out the possibility of the beneficial therapeutic effect of zinc supplementation in the management of leprosy. This is an aspect which would certainly merit further investigation.

It may be far-fetched in the present state of our knowledge to speculate if the high prevalence of leprosy in the South and the Eastern sea-board of India is in any way related to regional differences in dietary intakes of zinc arising from regional variations in soil zinc. We have no data at present to justify such a speculation. Indeed, available data do not point to the positive correlation between soil zinc levels and leprosy endemicity in the country.

Under the circumstances, the practical significance of the biochemical changes reported by Saha and Rao, from the point of view of etiology, pathogenesis and treatment of leprosy, would call for further intensive studies. We need to broaden our strategy for the prevention and control of leprosy instead of placing our entire reliance on multi-drug therapy of established cases. The "nutritional dimension" of the leprosy problem appears to be a somewhat neglected field which has failed to excite nutrition scientists. It is in this context that the work of Kunal Saha and his associates, briefly reported in this issue, assumes significance and importance. Their brief report may not do full justice to their rich contributions in this area. It is perhaps a reflection of our distorted priorities that work of this kind has attracted scant attention and little recognition. We most certainly need more studies of the kind now being carried out by Saha and Rao in order to be able to combat the problem of leprosy in an effective and comprehensive manner.

C. Gopalan

References

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