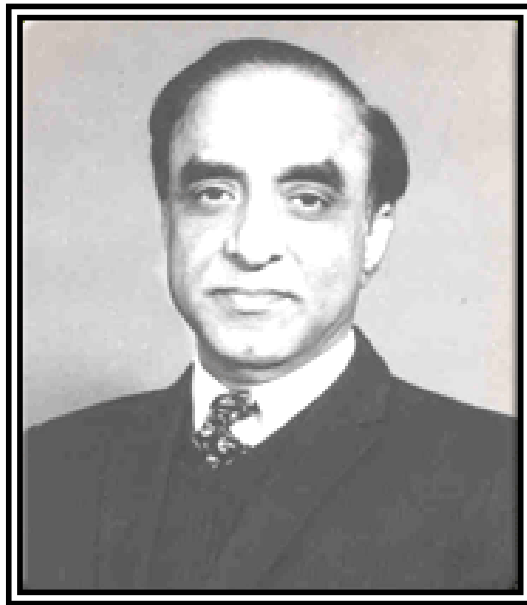


**SCIENCE FOR HEALTH AND NUTRITION SECURITY**

**A FESCHRIFT FOR DR C GOPALAN**



**NUTRITION FOUNDATION OF INDIA , NEW DELHI .  
2008**



## PREFACE

*The year 2008 is a major watershed year for all those who have known and worked with Dr. C. Gopalan. At the age of 90, he devotes more energy and time than most people half his age, to scientific scrutiny of existing and emerging nutrition problems and to passionate advocacy of appropriate interventions for improving the nutrition and health status of the citizens of India and other developing nations. What is the right way to celebrate the ninetieth birthday of this gentle giant who is seen by so many as the “Father of Nutrition”? We wrote to his colleagues, friends and students in India and abroad to ascertain the most appropriate way for us to celebrate this milestone, and to ask whether they would contribute articles for a Festschrift for Dr. Gopalan.*

*The response we received was immediate, positive and enthusiastic. The warmth and affection evident in the responses from people belonging to three different generations across the globe is the best testimony to Dr. Gopalan’s unique global, trans-generational appeal to the minds and hearts of all those who have come in contact with him. Over the past four months the articles for the Festschrift flowed in. These covered an impressive range: the authors’ personal reminiscences of their association with Dr Gopalan, their views on his contributions to the scientific and public health aspects of nutrition, and reviews of important nutrition issues in their respective areas of expertise. The contributions varied widely in length, content and style. We decided to keep the editing to the minimum in order to retain the flavour and diversity of the original contributions. We hope that the contributors will understand the challenges faced in editing such a diverse set of manuscripts, and will pardon us for inadvertent errors that we might have committed during editing.*

*We have somewhat arbitrarily divided the contributions into two parts: “Science for health and nutrition security” and “Felicitations” and arranged the contributions alphabetically. A third section entitled “Sixty years of distinguished leadership” gives some details of Dr Gopalan’s career and publications over the last six decades. We plan to upload the Festschrift on the web site of Nutrition Foundation of India so that this unique tribute to a living legend in the field of nutrition will be readily accessible to any interested reader in any part of the world.*

*Staff and Governing Body Members  
Nutrition Foundation of India*

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**Section – 1**

**SCIENCE FOR HEALTH AND NUTRITION SECURITY :  
A KALIEDOSCOPE OF VIEW POINTS**

# TACKLING IRON DEFICIENCY IN INDIA: A DIFFICULT JOURNEY

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## Introduction

Historically (1500 B C), in Ayurvedic literature, Charak samhita described fatigue and pallor caused by “bloodlessness”, which can be cured by Lauha bhasma (calcified iron). During the same period, the Egyptian manual of therapeutics ‘Ebers Papyrus’ described a disease characterized by pallor, dyspnea and oedema. In Greek literature (1554 – 1700) “Chlorosis/Demeorbo Virgineo” or green sickness was described as curable by drinking iron rust dissolved in water or wine.

In India, in 1968, Dr Gopalan constituted an Expert Committee of the Nutrition Society of India, to suggest measures to control anaemia in the country. The Committee, on the basis of the available data on prevalence and severity of anaemia from Delhi, Calcutta, Madras and Vellore, recommended the setting up of a National Nutritional Anaemia Prophylaxis Programme (NNAPP) for pregnant women as they were at higher risk of developing anaemia, possibly severe anaemia. The effort was a national commitment to prevent and control anaemia. Unfortunately, apathy towards the programme and disinterest in controlling iron deficiency made it a difficult journey to prevent nutritional anaemia and iron deficiency in the country.

## Current knowledge in the development of iron deficiency

Iron deficiency is an end result of a long period of negative iron balance, mainly due to poor dietary availability, rapid growth of the person, and blood loss. The pathological stages are;

- *Pre-latent deficiency*: Liver (Hepatocytes and macrophages), spleen and bone marrow show reduced iron stores (reduced- bone marrow iron and serum ferritin).
- *Latent deficiency*: With very low or absent bone marrow iron stores there is progressive reduction in plasma iron; the bone marrow receives little iron for haemoglobin regeneration (bone marrow iron is absent, serum ferritin is <12ug/l, transferrin saturation is <16% and free erythrocyte porphyrin is increased); however, hemoglobin concentration remains normal.
- *Iron deficiency anaemia*: this is a very late stage of iron deficiency with progressive fall in haemoglobin levels and mean corpuscular volume.

## Pregnancy outcome in anaemia

In the case of moderate to severe anaemia, breathlessness, oedema, congestive heart failure and even cerebral anoxia have been observed. Two hundred anaemic pregnant women observed in the University Hospital, Institute Medical Sciences, Varanasi, showed a higher incidence of premature

labour and of preterm, low birth weight and stillbirth deliveries. Even the infants born alive had low Apgar scores, and the rate of neonatal deaths was higher. Maternal mortality was 13 in 200 anaemic pregnant women as compared to 1 in 50 controls. Similar findings were reported in other Indian studies. Anaemic mothers do not tolerate blood loss during childbirth; as little as 150 ml can be fatal. Normally, a healthy mother during childbirth may tolerate a blood loss of up to 1000 ml<sup>1,2</sup>.

### **Iron deficiency in India**

As early as 1967, Routh & Agarwal<sup>3</sup>; studied the iron content in liver, spleen and muscle of healthy rich persons who died in car accidents on the streets of Delhi. It was found that >65% of these healthy persons had nil or very low iron content in hepatic tissue, indicating a severe degree of iron deficiency in our well-to-do population of Delhi. Later, in 1989<sup>4</sup> national studies by the Indian Council of Medical Research (ICMR)- covering 11 States reported that the prevalence of anaemia (arrived at by estimating haemoglobin using the cyanmethemoglobin method) in pregnant rural women was 87.6%, the mean haemoglobin level being <10.9g/dl. In six of the States, the anaemic women were given various doses of oral iron, 60, 120 and 180 mg, along with 500 µg folic acid daily for 90 days. In the year 1992, 62% continued to be anaemic in spite of receiving iron-folate therapy for 3 months<sup>5</sup>. This indicates that short-term treatment as recommended in the National Anaemia Control Programme may not be sufficient to control anaemia in pregnancy. However, it was observed that birth weights improved and the incidence of low birth weight deliveries was significantly reduced<sup>6</sup>. Gomber *et al.*, in 2002<sup>7</sup>, showed that pregnancy anaemia affects foetal growth. They administered a high dose (335mg) of ferrous sulphate and 500µg of folic acid for 14 weeks as either weekly or daily doses. Both dosing regimens were effective in controlling pregnancy anaemia, thereby suggesting, that the administration of even a once-weekly iron- folate dose can be effective.

The National Family Health Survey 1998-99 (NFHS-2)<sup>8</sup>, using the hemocue method for estimation, reported the prevalence of anaemia as 49.7% in pregnant women, 56.4% in breastfeeding non-pregnant women, and 50.4% in non-pregnant non-breastfeeding women. The hemocue method over estimates haemoglobin level, and it is therefore difficult to compare these data with those from other national studies. Dr Gopalan raised two questions in relation to the NFHS-2 data

- Why not determine the prevalence and severity of anaemia in the same States/districts and villages covered by the NFHS-2, but this time using the cyanmethemoglobin method? The planned study was for observing the changing trends in anaemia over the years in the light of the earlier data collected using the cyanmethemoglobin method.
- What are the factors responsible for inter-State differences in the prevalence and severity of anaemia?

In 2002-2003, the Nutrition Foundation of India studied the prevalence of anaemia in pregnancy and lactation in 7 States (Assam, Himachal Pradesh,

Haryana, Kerala, Madhya Pradesh, Orissa, and Tamil Nadu). The prevalence of pregnancy anaemia was 86.1% (Hb <7.0g/dl- in 9.5%), and in lactating mothers with infants under 3 months of age, it was 81.7 % (Hb <7.0g/dl in 7.3%). The inter-State differences that were responsible for the differences in the prevalence rates of anaemia were mainly fertility, women's education, nutrition status and occupation, availability of antenatal services and iron folate tablets during pregnancy<sup>9</sup>.

In 1999-2000, the ICMR conducted a District Nutrition Survey in 11 States covering 19 districts. The prevalence of pregnancy anaemia was 84.6% (Hb <7.0 g/dl-in 9.9%). These study workers also found that 90% of the adolescent girls in these districts had anaemia<sup>10</sup>. Similarly, in East Delhi schools, 85% of the adolescent girls were iron-deficient and 49% were anaemic<sup>11</sup>. In an ICDS block that has been in operation for more than 20 years in East Delhi, >87% of the under-three age group of children were iron-deficient<sup>12</sup>, and >40% had vitamin B<sub>12</sub> deficiency. The above studies clearly show that our populations live with anaemia throughout the entire lifecycle, endangering child growth and development.

### **Effect of maternal iron deficiency on foeto-placental unit**

The high prevalence as well as the severity of anaemia during pregnancy and lactation carry grave connotations. This is the period when a baby's brain cells grow, neurotransmitters develop, and iron is essential for this process. Normally 'Placental Iron transfer' to fetus becomes 3 to 4 times during 20-37 wk of gestation. Cord serum iron and haemoglobin were found to be lower in pre-term as well as full-term infants of hypoferriemic mothers. There is an increased gradient, in the presence of maternal iron deficiency, for transport of iron from mother to foetus, but the transport remains proportional to the degree of maternal hypoferriemia. The placenta plays an important role in maintaining iron transport to the foetus. This process of iron transport is purely a placental function over which mother and foetus have no control; in fact, it has been shown that the placenta continues to "trap" iron even after the foetus is removed in animals<sup>13</sup>. In spite of this efficient protective mechanism, the placental iron content is reduced significantly in maternal hypoferriemia<sup>14, 15, 16</sup>. This was a very important finding, as earlier studies<sup>17</sup> by Vahlquist (1941) and Rios et al. (1975)<sup>18</sup> on Swedish and American women had reported that cord iron does not change in iron-deficient pregnant women.

The placentae of anaemic women showed a qualitative decrease in villous surface area, volume of villi and length of blood vessels, while surface area and volume of the intervillous space increased. These placental changes in anaemia did not normalise after rehabilitation,- suggesting that "maturational arrest" had occurred<sup>19, 20, 21</sup>. Foetal liver iron stores are reduced significantly in maternal hypoferriemia. Normally, the bigger the infant and more advanced the gestational age, the higher was the amount of iron in the foetal liver, spleen and kidney. The tissue iron content increases steeply in the last 8 weeks of gestation. Infants born before 36 weeks of gestation had half the iron content in hepatic reserve<sup>22</sup>. The iron content in breast milk is higher in hypoferriemic mothers, a phenomenon of "Physiological Trapping"<sup>23, 24</sup>.

## **Foetal brain iron content in maternal latent iron deficiency in rats**

Iron as a micronutrient is required for the regulation of brain neurotransmitters by altering the enzymatic pathway system. In order to study iron deficiency, a rat model was developed to create iron deficiency (low hepatic iron) without change in haematocrit levels. In postweanling rats, iron decreased irreversibly in all brain parts except medulla oblongata and pons. Susceptibility to iron deficiency showed variable reduction in different parts of the brain:- corpus striatum 32%, midbrain 21%, hypothalamus 19%, cerebellum 18%, cerebral cortex 17% and hippocampus 15%. Alterations in brain iron content also induced significant alterations in the percentages of Cu, Zn, Ca, Mn, Pb and Cd<sup>25</sup>.

## **Foetal latent iron deficiency and brain neurotransmitters in rats**

Taneja<sup>26</sup> and Shukla<sup>27</sup> showed that in latent iron deficiency there is irreversible reduction in:

- brain 'glutamate metabolism'-(GAD, GDH, GABA-T); there was a marked reduction in the levels of brain GABA, L glutamic acid and enzymes for biosynthesis of GABA and L-glutamates like glutamate decarboxylase and glutamate transaminase; the binding of H<sup>3</sup>Muscimol at pH 7.5 and 1mg protein/assay (GABA receptor) increased by 143% , but glutamate receptor binding decreased in the vesicular membranes of latent iron-deficient rats by 63%<sup>28</sup> .
- brain 'TCA-cycle' enzymes; mitochondrial NAD+ linked dehydrogenase reduced significantly
- brain 'Catecholamine metabolism'; whole-brain-dopamine, neonephrine, tyrosine and TAT reduced significantly; in the corpus striatum the situation was similar, except that TAT increased.
- brain '5-HT metabolism'; tryptophan, 5-HT, and 5-HIAA reduced significantly.

The whole-brain and corpus striatum showed reduction in catecholamine, dopamine nor-epinephrine, tyrosine and monoamino oxidase, while tyrosine amino transferase increased in the corpus striatum in spite of reduction in whole-brain, thereby suggesting that latent iron deficiency induces irreversible neurotransmitter alterations. These changes were specific to iron deficiency, because neurotransmitter alterations in the foetal brain on account of malnutrition get normalised partially or completely on rehabilitation<sup>29, 30</sup>. The significant effects on neurotransmitter receptors (glutamate mediators) during the early stages of iron deficiency clearly indicate the deficits in both excitatory and inhibitory pathways of the central nervous system, showing that iron plays an important role in brain development<sup>25</sup>.

To test the above findings in humans, babies born to moderately-to-severely anaemic mothers were examined for "impact of iron deficiency on mental functions". The intrauterine-growth-retarded offspring of anaemic and undernourished mothers showed:

- hypotonia in 72% and hypoexcitability in 56%
- modification of responses in several neonatal reflexes, e.g. limp posture, poor recoil of limbs, and incomplete Moro's and crossed extensor responses.
- shortening of sleep cycle (REM and NREM) as evidenced on the EEG, the reduction being more marked for REM sleep. There was some inter and intra-hemispheric asymmetry and abnormal paroxysmal discharges, suggesting dysmaturity of the brain<sup>31, 32</sup>.

The above findings were not specific to the effects of anaemia on mental functions. Therefore the effects of anaemia (nutrition-controlled) on mental functions were then studied separately in rural children during a period of three years, with the support of the Nutrition Foundation of India.

Mental functions in nutrition-controlled 388 rural primary school children (6-8 yr of age), matched for social and educational status, were studied by WISC and arithmetic test to assess "intelligence, attention and concentration". Anaemia does not affect intelligence, except subtest-digit span. In arithmetic tests, attention and concentration was poor in anaemic children<sup>33</sup>.

### **Anaemia and brain-MRI studies in humans**

In anaemia caused by iron deficiency (serum ferritin <15µg/l) there is nil or low iron content in body tissues. By contrast, in thalassemia (>1000µg/l), there is excess of iron in body tissues. The iron content on globus pallidus, caudate and dentate nuclei was similar in both the clinical conditions, indicating that the deposited iron in brain does not change. In anaemia there was an increase in creatinine and aspartate and reduction in choline concentration. These are significant findings, as choline is synthesized in the brain in very small amounts; its uptake is Na<sup>+</sup>-dependent, requiring oxygen. Such changes are also observed in Huntington's chorea and Alzheimer's disease<sup>25</sup>.

### **Effects of iron deficiency and/ or anaemia on the brain**

Iron-deficiency anaemia in infancy has been consistently shown to negatively influence performance in psychomotor development. Short-term iron therapy did not improve the lower scores, despite complete haematological replenishment. Neurological maturation was studied in infants 6 months of age, including auditory brain stem responses and nap time 18-lead sleep studies. The central conduction time of the auditory brain stem responses was slower at 6, 12 and 18 months and at 4 years in these children, despite iron therapy having commenced at 6 months. During the sleep-wakefulness cycle, heart rate variability, - a developmental expression of the autonomic nervous system, was less mature in anaemic infants. This is possibly due to altered myelination of the auditory nerves<sup>34</sup>.

Lozoff *et al*<sup>35</sup>, in their studies on the long-term effects of iron deficiency in infancy; showed that these children, from preschool to adolescence, had poor cognitive, motor, and socio-emotional function, as well as persisting neurophysiological differences (slow transmission of nerve impulses



throughout the brain in auditory and visual systems). This is due to defects in myelination, neurometabolism and neurotransmitter function in iron deficiency. It has been observed that these changes are resistant to iron therapy in children <2 years of age with iron-deficiency anaemia, but not in older children<sup>36</sup>. These studies supported our earlier findings that brain functions are significantly affected in latent iron deficiency in the brain growth period, and that such changes are irreversible. These findings have serious consequences, e.g. poor cognition and learning disabilities.

The above research studies by our group are mainly on the effects of latent iron deficiency on irreversible brain function, and neurotransmitter alterations in the brain growth period. Once anaemia sets in, the additional effects are due to anoxia. Our nation is faced with the problem of iron deficiency that leads to anaemia, a clinical condition caused by the deficiency of many nutrients, mainly iron, folic acid and vitamin B<sub>12</sub>. Folic acid is essential from the prenatal period onwards, and its deficiency causes neural tube defects. In India, the population experiences a whole life cycle of anaemia, endangering child growth and development. Nutritional anaemia is treatable as well as preventable, and the available control measures are affordable. Let's do it now.

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# POPULATION STABILISATION: ISSUES AND CHALLENGES

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## Introduction

According to the 2001 Census, India's population was 1,028,737,436 (~102.9 crores). Viewed globally, India represents 16.9% of the world population and 2.4% of the global land area. Currently (2008) India's population is estimated at 114.7 crores.

Years	Total Population (in Crs.)	Absolute increase (in Crs.)	Decadal Growth Rate	Average Annual Exponential Growth Rate	Phase of Demographic Transition
1901-1951	23-36	13	-	-	Near stagnant population
1951-1961	36-44	8	+21.6	1.96	High Growth
1961-1971	44-55	11	+24.8	2.22	Rapid High Growth
1971-1981	55-68	13	+24.6	2.20	
1981-1991	68-84	16	+23.9	2.14	High growth with definite signs of fertility decline
1991-2001	84-102	18	+21.3	1.93	

*Source: Reference 1*

The population of India grew by 21.6% in the first decade after Independence; the rate rose to 24.8% during the next decade. The growth began declining from the third decade onwards, and in the decade of 1991-2001 it declined to 21.3% (Table 1)<sup>1</sup>. Despite the fact that the population growth rate in India has been declining steadily over the last two decades, the population size is increasing because of the high proportion of young people in the reproductive age group. India's population growth can be compared to a fast-moving express train, which has applied its brakes but cannot stop immediately because of its momentum. The population size will continue to grow for some more time because of the "*population momentum*" factor.

The current high population growth rate in some parts of the country is due to the large size of the population in the reproductive age group, higher fertility due to unmet need for contraception, and desire on the part of parents to have more children in the light of the prevailing high Infant Mortality Rate (IMR). India is a country of striking demographic diversity. Substantial differences are visible between states in the achievement of basic demographic indices. This has led to significant disparities between states in respect of current population size and the potential to influence population increase in future. The population growth rates continue to be high in the states of Bihar, Uttar Pradesh, Madhya Pradesh and Rajasthan. These states with high fertility rates are the very ones with low literacy rates and poor health indicators high infant mortality and high maternal mortality. These states account for nearly 40% of the country's population and will contribute

well over 50% of the growth in the coming decades. Their performance and the demographic outcomes will determine the time point and the size of population at which India will achieve population stabilization.

## Future projections

As per the report of the Technical Group on Population Projections set up by the Office of the RGI:

Sl. No.	India and Major States	Year by which projected TFR will be 2.1
	India	2015
1	Andhra Pradesh	Achieved in 2002
2	Assam	2019
3	Bihar	2021
4	Chhattisgarh	2022
5	Delhi	Achieved in 2001
6	Gujarat	2012
7	Haryana	2012
8	Himachal Pradesh	Achieved in 2002
9	Jammu & Kashmir	NA
10	Jharkhand	2018
11	Karnataka	Achieved in 2005
12	Kerala	Achieved in 1993
13	Madhya Pradesh	2025
14	Maharashtra	2009
15	Orissa	2010
16	Punjab	Achieved in 2006
17	Rajasthan	2021
18	Uttar Pradesh	2027
19	Uttarakhand	2022
20	Tamil Nadu	Achieved in 2000
21	West Bengal	Achieved in 2003
22	North East (Excl. Assam)	Achieved in 2005

Source: Reference 2

- The population of India is expected to increase from 1029 million to 1400 million during the period 2001-2026 an increase of 36% in twenty five years at the rate of 1.2 % annually.
- The Crude Birth Rate will decline from 23.5 in 2006 to 16.0 during 2021-25 because of falling levels of total fertility.
- The Infant Mortality Rate, which is reported to be 57 in 2006, is expected to decline to 40 by the end of the period 2021-25.
- With declining fertility and increasing life expectancy, the number of older persons is expected to double from 71 million in 2001 to 173 million in 2026.
- The proportion of the population in the working

age group 15-59 years is expected to rise from 57.7 percent in 2001 to 64.3 % in 2026.

- The population in the school-going age of 5-14 years is expected to decline from 243 million in 2001 to 222 million in 2026.
- Out of the total population increase of 371 million between 2001 and 2026, the share of the workers in the age-group 15-59 years in this total increase is 83%. This has implications for the productivity of labour in future.
- The sex ratio of the total population (females per 1000 males) is expected to decrease (i.e. fewer females in proportion to males) from 933 in 2001 to 930 during 2026.
- The urban population in the country, which was 28% in 2001, is expected to increase to 38% by 2026.
- The Total Fertility Rate (TFR) is expected to decline from 2.8 in 2006 to 2.0 during 2021-25. The assumption is that the Total Fertility Rate would decline steadily and would touch the floor value of 1.8 in some States.

With this, the weighted TFR is projected to reach the replacement level of 2.1 by 2021 (Table 2)<sup>2</sup>.

It may be noted from the projections that India's population will reach replacement levels of TFR 2.1 in the year 2015, while some of the large northern states namely, Uttar Pradesh (UP), Rajasthan, Bihar and Madhya Pradesh (MP) will reach that level after 2021, in fact UP will reach only in 2027.

The reasons for extremely slow progress in population stabilisation and poor performance in provision of Reproductive and Child Health (RCH) services are complex and deep rooted. On the one hand, high rates of poverty and illiteracy and low levels of autonomy for women lead to poor knowledge of and low demand for RCH services. On the other hand, poor infrastructure and less-than-efficient governance compound the problem. Bridging the gap would require public awareness, sensitising administrators, and encouraging meaningful community involvement in the delivery of health services.

A major challenge for the States of UP, Rajasthan, Bihar and MP is to achieve population stabilisation. In these States, much needs to be done to address the unmet need and stabilise the population so as to earn benefits from the demographic dividend. The British Parliamentarians' report on "Return of the Growth Factor: Its Impact on Millennium Development Goals' is all the more relevant in the context of these States. Historically, India's population stabilisation efforts have centred around family planning, with focus on fertility reduction. Such narrow vertical programmes, often limited to achieving numerical targets, are not the answer for achieving India's population stabilization. Population stabilisation is not merely about numbers; it has to be looked at in the context of wider socio-economic development. It does not matter if in the process we don't stabilise by 2045 (as indicated in NPP, 2000), it could be achieved by 2050 or 2060. But what is of greater concern is how we approach the issue of population stabilisation. It should be a gender-balanced approach.

The "two-child norm" implies that the state promotes the ideal of two children per family and has a system of incentives and disincentives/punishments for achieving it. A "two-child norm" has the potential to cause immense harm to women's health in the existing social situation, where preference for a male child is high and women's status is very low. One of the important risks includes increase in sex-selective abortion and consequent reduction in the number of girl children.

There exists a linkage between social development indicators, health status and population stabilization. The issue of population stabilization is not a technical issue with a technical quick-fix solution. The answer does not lie in pushing sterilizations and chasing targets in the conventional mode. For achieving population stabilization, it is important to improve people's access, particularly women's access, to quality health care. The contraceptive mix needs to be enlarged and expanded. We are now discovering that the obvious route to population stabilization is through social development, through

women's empowerment, and through greater gender equality. It is being increasingly recognized that social investments help reach the goal of slower population growth. Improving health care, education and opportunities for women is a matter of human rights. It also empowers women and results in smaller and healthier families. All those who have worked for the cause of health and family planning understand that family planning is not an isolated programme, but has to be part of a comprehensive primary health care package within the overall gamut of social development.

The high-fertility districts are precisely the districts where all social and health indicators and the governance system are extremely poor. The social and developmental issues, including poverty issues, need to be tackled in a comprehensive and holistic manner rather than targeting population control / family planning on a stand-alone basis. It is therefore suggested that family planning and other population stabilization programmes should form an integral part of the comprehensive primary health care programmes and need to be based on "community needs assessment", which should be the starting point in any exercise of planning and designing of programme implementation.

Micro planning, involving an assessment of the community's needs, can help to identify and address the local problems through more acceptable strategies. Gender concerns and women's health concerns could be better taken care of in such a decentralized approach. The twin issues of gender and equity should be over-arching while implementing the National Population Policy (NPP). Quality of Care (QoC) should be an important issue to ensure mass appeal of the programme so that people utilize the facilities, assured of the quality in response to their felt need. Thus, in the planning stage itself, certain minimum and practical indicators of QoC should be incorporated. It is vital to install a good Management Information System (MIS) for improving the effectiveness of the programme. The emphasis on complete registration of births, marriages, pregnancies and deaths will serve to inform the planners of the current and the future status of the population and help at various stages of the programme.

Locating the Family Planning Programme in the Reproductive Health and Rights perspective, as a component of the comprehensive Primary Health Care, would improve the overall socio economic development of the country and ultimately stabilize population. India is at a stage of demographic transition and is indeed in the midst of a process where it faces the window of opportunity created by the demographic dividend/advantage. During the first three decades of post-Independence development, while Infant Mortality Rate (IMR) fell significantly, the fertility rate remained more or less stagnant. This led to a significant increase in the proportion of young people in the total population. There are about 331 million (33.1 crore) young people (in the age group 10 to 24 years) in India, representing a little less than one-third of the total population. This group is the largest generation of young people India has ever had. Recently a view has gained ground that what matters is not the size of population, but its age distribution. A population 'bulge' in the working age groups, however large the population, is an inevitable advantage.

One-third of India's population was below 15 years of age in 2001. In 2021, the average Indian will be only 29 years old, compared with 37 in China and the USA, 45 in Western Europe and 48 in Japan. The demographic process this implies would create a large and growing labour force, which is expected to deliver unexpected spin-offs in terms of growth and prosperity. Preparing the young people to be healthy and productive is critical for utilizing the available window of opportunity. We cannot and should not miss this opportunity.

India is emerging as a regional (or even global) power in the not too distant future. The demographic advantage or dividend to be derived from the age distribution in the population is traced to the fact that India is (and perhaps will remain for some time) one of the youngest countries in the world. Therefore, in our country, investing in young people equitably in their education, nutrition, skill, employment and health assumes special urgency and importance. Clearly a failure to do so will have long-term repercussions on individual lives, health systems, security, demography, economy and development. The population of India could be its biggest asset if appropriate policies and programmes are formulated and implemented with people's participation. We can reap the demographic dividend, as we stabilize population over the next 50 years.

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# **NUTRITION AND AGEING**

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## **Introduction**

Whenever we take up the question of ageing we have to remember that India is passing through a demographic transition, which is commonly known as “Pyramid to Pillar”. In other words, the numbers of elderly persons are increasing at a much faster rate than the general population – a structure that was earlier regarded, as a pyramid is now the shape of a pillar. In this phenomenon, the female elderly are increasing faster in number and, because they tend to live longer, they are experiencing various degenerative conditions. Why are the elderly people increasing faster in number? The simple reason is the reduction in death rate and consequently a longer life span due to better health care and health promotion. Similarly, the relative reduction in the population of the younger age groups is due to vigorous campaigns for reduction in birth rate.

A look at the demographic transition demonstrates that elderly persons often go on to become centenarians. Countries that have a rapid increase in the numbers of the elderly have a large number of aged persons at various stages of ageing: the “young old”, the “very old”, the “old old” and the centenarians. Today, the Japanese have the longest life expectancy and the centenarians in that country outnumber those in any of the other developed countries. Ageing is a phenomenon that has several features; ageing is inevitable, irreversible and invariably leads to senescence.

## **Chronological and biological aging**

In spite of various studies in different disciplines no one is able to find out the exact cause of ageing, though numerous hypotheses have been put forward from time to time. Ageing is broadly divided into two categories:

- chronological ageing according to the calendar and
- biological ageing which has no direct correspondence with chronological ageing but is consistent in every individual in every anatomical organ and physiological system. Chronological and biological ageing do not always coincide. For instance, a man might be 80 years old chronologically, but in terms of physiology his system and organs might be much younger or older.

Biological ageing occurs in every individual. It is a known fact that, with age, several organs and physiological systems undergo degradation. It is known that as a person ages he or she may:

- develop diabetes;
- develop cardiovascular disorders and hypertension;
- experience atrophy of the taste buds, especially those relating to sweet taste, thereby leading to an increased craving for sweets;



- develop irritability or “laziness” of the gastrointestinal system, resulting in flatulence and constipation.

Other abnormalities are also seen in those of advanced age. For instance, stones may develop in many organs, the urinary bladder gets atrophied. A better understanding of the processes and mechanisms underlying some of these changes associated with ageing may lead to providing a better quality of life to the world’s growing population of the elderly.

# **JOURNEY FROM LAB TO LAND: MOMENTS TO CHERISH**

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## **Introduction**

In every one's life there are moments and events, which are turning points and watersheds in time. For me personally, these events have all proved to be happy ones which have given the right direction to my life and helped me to be associated with institutions and individuals that I cherish, - Dr. C. Gopalan being one such individual. In Mrs Seetha Gopalan I have found a dear friend. At my age of seventy-three, going down memory lane and sharing experiences can be forgiven.

## **Entering the fascinating world of biochemistry**

The option to study biology/chemistry/ biochemistry instead of medicine (the latter being the career chosen by my twin sister, Mahrukh,) was a deliberate one since I loved science, particularly physics and biology, right from my school days. After completing B.Sc. with chemistry and botany, I joined the G.S Medical College, Bombay, for M.Sc. Biochemistry, a course that had been started just a couple of years earlier. While chemistry was not my passion or forte, the very first class in Biochemistry, taught by Professor Datta at the Grant Medical College, Bombay opened up a fascinating world. He was among the best teachers I have ever known. Besides Prof. Datta we were taught by stalwarts like Professors Kamala Sohni, Magar (at Indian Institute of Science, Bombay), Professor Ray at Wilson College and many others.

## **From Bombay to Bangalore- a turning point**

Professor V. Giri, Head of the Department of Biochemistry, Indian Institute of Science, Bangalore, was the examiner for M.Sc. the year I qualified, 1957. After the *viva voce* examination, he asked me whether I would like to come to Bangalore to pursue research towards a Ph.D. at the Indian Institute of Science. I was delighted and excited. My mother and an old aunt were apprehensive, but finally it was decided that I could go, with my father accompanying me to Bangalore. To me that seemed reasonable and reassuring. At Bangalore, a cousin and an uncle of my mother came along with my father to settle me at the Institute. Three old men coming along to settle a Bombay girl who wore dresses instead of traditional saris became the talking point in the Institute (something I learnt about many years later through others). Professor Giri assigned me to Professor Homi Cama, a well-known scientist and a good man, who created a very happy working environment. He in turn suggested that I associate my self with P.R. Sundaresan who was working on a tough problem vitamin A<sub>2</sub> chemistry and metabolism. Purifying and crystallising vitamin A<sub>2</sub> was a challenging task, since vitamin A<sub>2</sub> is a very unstable compound, and there were moments of great frustration and anxiety. Long hours of work had to be put in. But finally things worked out and

classical papers emerged. In those days there was no shortage of power and water, but there was scarcity of equipment. There was only one Beckman Du spectrophotometer, the life-line for biochemistry research, to be shared between the departments of biochemistry and pharmacology, and it had to be booked ahead of time. Sometimes bookings were available only at night.

After Professor Giri passed away, Professor P.S. Sharma from Madras became the Head of the Department. The system of journal clubs was started. All the students had to come prepared with their papers and any one would be called to present it, using a black board and chalk. I discovered my ability to speak at the first journal club meeting, when stern Prof. Sharma, with a flicker of a smile complimented me.

In the early 1960s, Professor C.V. Raman developed a fascination for studying the role of carotenoid pigments in vision. This provided me an opportunity to interact with this great man. Though the theory that he proposed could not be proved, discussing science with a man like him was a wonderful experience. The obvious course after Ph.D. was to go to the US for Post-doctoral experience. I did the obvious, and had the great opportunity to work with Norman Krinsky, an authority on carotenoids at the Tufts University School of Medicine, Boston, and with Andre Jagendorf, an important name in the field of photosynthesis, at Johns Hopkins University, Baltimore. Those three and a half years in the US were delightful and a great learning experience. My friendship with Krinsky and Jagendorf and their wives has lasted over the years. In 1962, at Tufts University School of Medicine, I was the only woman post doctoral student. Edith Wilson (later Miles) came the following year, and my friendship with her and her husband Todd Miles also continues.

### **Back to India to Hyderabad**

Professor Sharma facilitated my return to India in October 1965 and advised me to write to Dr. C. Gopalan, Director National Institute of Nutrition (NIN), Hyderabad, for a job at NIN. Dr. Gopalan responded promptly to my letter and advised me to apply indicating the salary I expected. I was modest and asked for Rs 800/- per month. The selection committee, I am told, was impressed with my modest demand. I was offered the job with a salary of Rs 900/-. This turned out to be a typographical error, and the offered salary was only Rs. 600. However, I accepted. NIN had a friendly and welcoming atmosphere, a characteristic that has persisted over the years. Dr. Gopalan was charming and very supportive. Thus my 29 long years of association with NIN yet another watershed in time began.

Though Nutrition is an old science and the science of biochemistry began as nutritional biochemistry, vast gaps exist in our understanding of: the mechanisms of absorption and action of micronutrients at biochemical, cellular and molecular levels; tests for early detection of deficiencies; the biochemical and molecular bases of the pathology of nutrient deficiencies; nutrient requirements for preventing deficiency disease vs positive health; functional consequences of marginal malnutrition; interaction within nutrients

and between nutrients and other chemical and biological agents; and many others. The discovery of health-promoting phytochemicals (nutraceuticals) other than established nutrients has opened up the vast field of functional foods. The impact of nutrition on foetal programming, and long-term health consequences is yet another fertile area for research. To solve these problems at a basic level, the concerted efforts of medical professionals, biochemists, physiologists, and cellular and molecular biologists are required. At NIN I had an opportunity to foray into some of these areas.

### **Studies on B complex vitamins**

Dr. Gopalan got me started on developing biochemical tests for assessing vitamin B status. An enzymatic test for vitamin B1 (thiamine) had been described and all I had to do was to standardise it and apply it to find out the extent of thiamine deficiency in our population and use it to derive the thiamine requirement of Indians. Vitamin B2 (riboflavin) was another story. A good test had to be developed. I hit on the idea of testing the response of the enzyme erythrocyte glutathione reductase--a FAD-dependent enzyme. For years people were looking for a good test for assessing riboflavin status and strangely, when I got the idea, miles away D. Glatzle in Hoffman La Roche, Switzerland also thought of the same enzyme. This we learnt from Dr. Buzina who came to NIN to collect blood samples of Indians to test for riboflavin deficiency. Dr. Gopalan advised me to be careful. I was forthright and told Buzina that I had already standardised the test and got encouraging results. Both Buzina and Glatzle took it in the right spirit and we continued to exchange notes and learn from each other's experience. I even visited Glatzle's laboratory. Some of the depletion/repletion metabolic experiments that we did on human volunteers (including myself) to test the application of enzymatic tests for assessing B-vitamin status, and thereby deriving the requirement for humans, may not go through the present day Ethical Committee reviews easily. None of us, however, have suffered. My first student Sharda was a tireless and patient worker. She was the first of my students who stayed with me, a practice, which continued over decades; people used to tease me that I run a 'gurukul'.

NIN, with its varied expertise and access to clinical material, pathological laboratory and animal facility, offers a unique opportunity to undertake research on various aspects of human nutrition. Discussions with Dr. Gopalan were very refreshing because he quickly grasped new ideas and came up with useful and interesting suggestions. My only regret till this day is, I don't have a single publication with him as the co-author. That is also his greatness. Unlike other seniors who thrust their names into publications regardless of their contribution, Dr. Gopalan allowed his brain to be picked freely, but did not allow his name to be mentioned as author unless the original idea and guidance was his. As we all know, Dr. Gopalan is impatient and quick-tempered. So am I, and we did have differences of opinion. But my regard and respect for his intellect, understanding and commitment have grown over the years. The late Dr. Srikantia was different very intelligent and knowledgeable, but cool. Dr. Srikantia had a calming effect during moments of anxiety. I cherish my friendship with his wife Shanta as well. Besides Dr.

Gopalan and Dr. Srikantia, I learnt a lot about nutrition from other seniors and dear friends like Drs. Tulpule and Narsingha Rao and the late Drs. Bhavani, Ramasastry and Balasubramaniam.

The inspiration for some of my best work at NIN came from observations made in the clinic by clinician colleagues, or in the field. Drs. Leela Raman and Kamala Krishnaswamy observed that clinical lesions of the mouth such as angular stomatitis and glossitis most often responded to treatment with vitamin B2 and are generally attributed to vitamin B2 deficiency. However, sometimes-complete recovery is possible only with the administration of other B vitamins, particularly vitamin B6 (Pyridoxine). This got us started on studying the interaction between B-vitamins and the biochemical/molecular basis of the mucocutaneous lesions, which respond to treatment with these vitamins. The biochemical lesion for this pathology was found to be homocysteine accumulation in tissues, since B- vitamins are needed for metabolising homocysteine. Molecular lesion was found to be impaired collagen cross-linking in skin, since homocysteine inhibits the enzyme lysyl oxidase needed for collagen cross-linking. Our evidence-based hypothesis has not been disputed. The same biochemical pathology leads to impaired wound healing in the context of vitamin B deficiency.

Vitamin B2 fails to evoke public health interest since its deficiency does not cripple or kill. Yet bio-chemically it is very important, being required for energy transduction reactions in mitochondria and generation of ATP. In fact, we have observed that, in riboflavin deficient rats, ATP generation in mitochondria is affected. This may explain some of the adverse functional consequences of riboflavin deficiency, like reduced psychomotor function (hand steadiness) in children, and impaired phagocytosis.

In the process of testing the validity of the glutathione reductase test for assessing riboflavin nutrition status in rural school children, Dr. Rameshwar Sharma of the field unit and I found that, during winter months, urinary excretion of riboflavin shot up and this was associated with an increase in the incidence of respiratory infections. This chance observation was investigated through studies in slum children and a mouse model, thanks to help from Drs Bhaskaram (paediatrician) and Suresh (veterinary microbiologist) at NIN. We could show that respiratory infections affected the conversion of riboflavin to its co-enzyme forms FMN and FAD, and that this resulted in reduced binding of the vitamin to its apo-proteins, and also in a shorter half-life. This probably is the reason why the vitamin status of many poor children who are prone to frequent bouts of infection, fails to normalise even after supplementation.

Our group's research on the effects of contraceptive steroids on nutrition and health also began with an observation that women using oral contraceptives often develop oral lesions -angular stomatitis and glossitis. The biochemical basis of the side effects of contraceptive steroids on vitamin nutrition, glucose metabolism and liver regeneration were studied by doing experiments on animals and women. It was clear that these steroids increased the requirement of vitamins in women due to alterations in the levels of specific binding proteins. The biochemical basis of the altered glucose tolerance was

also elucidated. Dr. Prema Ramachandaran and I led a large WHO-sponsored international multi-centric study to investigate the safety of contraceptive steroids in malnourished women. Our conclusion was that these drugs are by and large safe at low dosages, but some micronutrient support to the women would be needed. Altered glucose tolerance in these women was not synonymous with developing diabetes, and was reversible. Nevertheless, the need for monitoring the health of women using contraceptive steroids cannot be overemphasised.

### **Studies on carnitine**

Another interesting line of research was to find out whether carnitine, which is synthesised from the essential amino acid lysine, is an essential nutrient. Carnitine is needed for the intra-mitochondrial transport of fatty acids for their oxidation. Experiments in humans and animals showed that indeed, in humans suffering from protein-calorie malnutrition and in rats fed on lysine-deficient cereal diets, the carnitine status is compromised and this can well be the basis of fatty changes in the liver in protein-calorie malnutrition. We showed that trimethyl lysine is an intermediate in the lysine-carnitine pathway. Carnitine research brought me in touch with Professor Harry Broquist of Vanderbilt University. Our friendship has also lasted over the years.

### **Other studies**

My work on the role of vitamin B deficiency in serum homocysteine, an independent risk factor for cardiovascular disease, was initiated just before my retirement. Despite some subsequent work by Drs AV Lakshmi and Kamala Krishnaswamy, that promising line of work is an unfinished agenda.

For several years, I had the opportunity to head the Laboratory Animal Information Service centre-LAISC (now renamed as National Centre for Laboratory Animals). Heading this organisation was a scientific and administrative learning experience, and I continue to champion the cause of ethically conducted animal experimentation for biomedical research.

I was fortunate to have wonderful students and colleagues. Space limitation prevents me from listing them, but special mention needs to be made of Dr. A V Lakshmi and Mr C M Jacob for their long association and contributions. Those were the days when NIN scientists enjoyed classical music. Thanks to Dr. K. T. Achaya (who is no more) who was at the RRL (Indian Institute of Chemical Technology, Hyderabad) some of us could attend both Hindustani and Carnatic music concerts, because he would offer to take us in his car. Dr Achaya, besides being a good scientist, was a culture vulture and I owe my appreciation of Carnatic music to him.

### **From lab to land**

My decision to move from the lab to the land despite not being trained for it was made during a visit to the Comprehensive Rural Health Project of Raj and Mabel Arole in Jamkhed, Maharashtra, with members of the Medico Friends

Circle. The Aroles have pioneered the training of even illiterate rural women as effective grass-root health workers. This was another turning point in my life. On retiring from NIN, instead of continuing with lab work, I decided to join my friend Dr. Devyani Dangoria and her establishment, Dangoria Charitable Trust (DCT). Devyani is a gynaecologist with a deep societal commitment. The Trust runs a hospital for women and children, and a home for the aged in village Narsapur in Medak district of AP.

Dr. Gopalan was not happy with my decision to leave biochemistry and go into field work. But once he saw my determination, he has been very supportive. Besides Dr. Gopalan, I have received a lot of encouragement and advice from Professor M S Swaminathan on whom I tend to unburden whenever I have a problem related to agriculture practices that are unfriendly to nutrition security. The constant encouragement and advice from other friends like Dr. S. Varadarajan, Professor MV Rao, Professor G Satyanarayana, Dr. V. Prakash, Prof. VLK Prasad, Sri Narasimha Reddy, Drs Prema Ramachandaran, T P Susheela, and colleagues at NIN, DCT, CFTRI, and other scientists and relatives has also helped to sustain my enthusiasm.

I was fortunate that ICMR gave me an Emeritus Scientist position with placement at this less-known NGO. The Department of Science and Technology (DST) and the Department of Biotechnology (DBT), Government of India, have largely funded our projects relating to science and society.

Nutrition is not a stand-alone subject. To impact on nutrition delivery there has to be convergence between Awareness, and Access at Affordable cost to balanced diet (food security), and healthy environment including clean drinking water, and access to health care (nutrition security). My right-hand man, PVVS Murty (a social scientist) and I have tried to evolve models for each of these, while working in the villages around Narsapur, Medak district, AP. Our model of Health and Nutrition Entrepreneur and Mobiliser has helped to reduce perinatal, neonatal and infant mortality, and also made a small impact on child nutrition and birth weight. For improving food security, our effort has been to promote diversification: moving from mono cropping with paddy and sugar cane to horticulture, legumes and millets, and crop-livestock mixed farming using green methods. A food-processing-cum-training centre has been established, with financial support from the Ministry of Food Processing Industries (besides DST and DBT) in collaboration with CFTRI, Mysore.

Dr. Gopalan keeps raising the question: how relevant are these small experiments in the larger context? Can they be scaled up? I don't have the answer except to quote:

*“ I am only one, but still I am one. I cannot do everything, but still I can do something; and because I cannot do everything I will not refuse to do something that I can do.” Helen Keller.*

## ON NUTRITION SECURITY

Bhargava P M

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*My first meeting with Gopalan was in the late 1950s when V N Patwardhan was the Director of the National Institute of Nutrition (NIN), which had just shifted to Hyderabad. I, in fact, attended the Foundation Stone laying ceremony of the NIN some five decades ago. I was surprised by Gopalan's attention to detail, lust for work and life, and a global futuristic view of science in which all knowledge was integrated. Having just made a transition from physics, chemistry and mathematics to biology which I had never studied, I had realized that nature does not compartmentalize knowledge. It was a delight to recognize that, in Gopalan, I had a friend in this belief.*

*Patwardhan was like a saint: totally focused on work and benevolent to a fault. He was simplicity personified; he managed to lead, it seemed to me at that time, an uncluttered life. I recall many visits to his house in Marredpalli. He was as far away from glamour as anyone can be. Gopalan and I were, on the other hand, fascinated by the glamour of science and the ever-increasing dimensions of life. I like to dress well, but could never beat Gopalan who was always meticulously dressed even when he came to our house in the campus of the then Regional Research Laboratory (now IICT) on Sunday mornings. With his good looks, he could easily pass off as a playboy!*

*When he became the Director of NIN – a logical successor to Patwardhan – NIN was transformed: not only a new coat of paint but a new vibrant culture, opening new frontiers for scientific investigation. I particularly remember the Sunday morning visits to each other's houses, both his wife and he being super hosts. I remember he and his wife being with us when we were living in a house near Engineering College of the Osmania University (before we shifted to the house in the RRL Campus), on 21<sup>st</sup> April 1961. It was the biggest birthday celebration in our family, being the first birthday of our first child. I remember that nothing escaped Gopalan's notice and his compliments were a testimony of his intense perception and attention to details. He was the only one out of over a hundred invitees who recognized that the invitation card was something unusual as was the way the tables were laid and the plants lit up.*

*His grasp of the science of nutrition and its relationship to other biological sciences is well known and widely recognized through the numerous awards and honors he has received, including the Fellowship of The Royal Society and, before that, his appointment as the Director General of ICMR. But I do not believe our Government ever recognized his other outstanding qualities. He should have been the Nutrition Advisor to the Government of India, all the departments of which, as of now (unfortunately), serve food at their meetings, which would be least appropriate for the age group that generally attends these meetings! I have always admired Gopalan's resilience: the way he extricated himself from the quagmire of personal grief, which would have virtually killed lesser people. His great determination has been exemplary. Indeed, for my wife, and me it has been a matter of great pride to have known*



*the Gopalans whom we have always considered as very good friends. Gopalan and I shared, among other things, a strong commitment to nutrition security in the country. I would, therefore, on this occasion, like to share with the readers (as my tribute to Gopalan) my current concern in this area and some related ones.*

## **Introduction**

Nutritional security means enough food and the right kind of food for every citizen of the country. It, therefore, relates to food security. And food is produced by farmers who live in villages that is, our rural sector. Therefore, in my perception, nutrition security, food security, farmers' security, agriculture security and security of our rural sector are functionally synonymous. In other words, neglect of the rural sector implies neglect of farmers and, therefore, of agriculture. And lapses in agriculture mean less food – both in quality and quantity. In an ideal situation, people like Gopalan would tell us what kind of food we need to grow to ensure that every one has enough food and the right kind of food. But that wouldn't be enough, unless we provide security to agriculture, to the farmers and to our rural sector.

## **Food and nutrition security**

I believe agricultural security and, therefore, food and nutrition security as well as the security of farmers and the rural sector, is comprised of the following 19 components:

- Good and appropriately priced seeds, a network of seed-testing laboratories accessible to farmers and progressive replacement (through research) of hybrid seeds with seeds that breed true and technologies such as apomixis, so that farmers can use their seeds.
- Strategies such as integrated pest management that would minimize the use of chemicals such as pesticides; and judicious use of agro-chemicals so that they do not contaminate soil and water as they are doing today.
- Assured and quality power (but not free power), adequate water, and judicious use of both water and power.
- A network of soil testing laboratories easily accessible to farmers, particularly to ensure that the soil has all the required micronutrients.
- A judicious mix of traditional and modern agricultural practices. Examples of traditional agricultural practices would be organic agriculture and use of biopesticides. The ICAR has, in fact, put together, in a series of books, over 4,000 traditional agriculture practices of which nearly 100 have been validated and some 40 cross-validated.
- Both *de jure* and *de facto* empowerment of Panchayats and women.
- A system that would ensure that farmers are able to market their produce at fair and remunerative prices.
- Sources of augmentation of income of agriculturists and village dwellers such as traditional arts and crafts; medicinal plants; world-wide use of our enormous repertoire of fruits and vegetables; organic farming; use of appropriate post-harvest technologies in a way that the primary producer becomes an important stake holder in the entire chain from production to

marketing of the processed food material; intelligent energy use, including use of energy-saving devices and protocols; strengthening of our animal husbandry through use of modern technologies; use of our marine wealth through, for example, marine biotechnology; exploitation of some 650+ varieties of orchids in, say, Arunachal Pradesh, for which tissue culture technology is available; and mushroom culture.

- Knowledge empowerment of the rural sector. In the short term, this can be done through information packages for Panchayats, exploiting their extensive and varied experience. In the long term, there is no substitute for free and quality education to every rural child (as in the case of urban children) up to class XII, and ensuring the availability of enough quality vocational training institutions, including for traditional technologies such as hand-made textiles. This cannot happen unless we decommercialise school education as well as higher education at least up to the degree level.
- An appropriate system of providing loans to farmers at low rates of interest, such as a micro credit system.
- Integration of rural and urban sectors through roads, communication channels, medical and health care, and setting up of appropriate industries in the rural sector. As regards medical and health care, preventive steps would be provision of safe drinking water, of vaccines, of good nutrition to ensure (for example) that each individual receives enough iodine, iron, vitamin A, protein and calories; expansion of the public distribution system to include grains other than wheat and rice could help a great deal. As regards provision of medical and health care to the rural sector, one would need to set up an effective three-tier system, the first two tiers to be provided by the Government and the third tier by the private sector through insurance cover. The first tier may not require doctors who have a regular medical degree. (A model has been worked out for such a three-tier system.)
- It has to be ensured that when policy decisions such as the National Rural Employment Guarantee Scheme are taken, they are appropriately implemented.
- There are a number of areas in the field of agriculture where either new work needs to be done or existing work needs to be widely disseminated. In fact, we have elsewhere listed 20 such areas of which a copy has been also sent to the Prime Minister. Examples would be introduction of hybrid vigour into poor breeding varieties or propagation of hybrids through apomixes and development and propagation of technologies for controlled release of fertilizers and pesticides.
- Immunity from external threats, such as
  - high-pressure marketing of seeds that we do not need, by multinationals who have dug their way through the web of politicians and bureaucrats by bribing;
  - sale of spurious agrochemicals or agrochemicals that are simply not necessary, through high-pressure advertising and connivance with official channels;
  - uncalled-for import of agricultural and other food products, an example being the import of wheat in 2007 and 2008; and

- our country signing international agreements which give a lot of concessions to Governments and multinational corporations outside India with little benefit (if any) to our country, such as the recent Indo-US Knowledge Initiative in Agriculture or the Indo-US CEO Agreement.
- A system to predict and manage disasters such as floods, droughts and famines. India may be the only country where in the same region and in the same year we have drought at one time and floods at another.
- Straightening out of land records and ensuring equitable and fair land distribution.
- An appropriate insurance against bio-terrorism, which can ruin our plant and animal wealth. Remember what Agent Orange made by Monsanto and used by the US in Vietnam during the US-Vietnam war, did to Vietnam's economy.
- A system to identify in real-time and deal with rare, emerging, new and exotic diseases of plants and animals, by setting up a Centre for Animal Disease Control and a Centre for Plant Disease Control on the lines of the Centre for Disease Control (for humans) in Atlanta, Georgia, USA. The High Security Animal Laboratory of the ICAR at Bhopal could be converted into the proposed Centre for Animal Disease Control.
- Appropriate steps to deal with progressive climate change, remembering that one degree rise in temperature can lead to a reduction in wheat production to the tune of 5 million tonnes.

We have the capacity to accomplish all these objectives. What is needed is a social, political and economic will to build on Dr.Gopalan's legacy to ensure nutrition security for the country on a long-term sustainable basis.

# JOURNEY FROM ERA OF FOOD TOXINS TO FOOD SAFETY: FIFTY YEARS OF CONTRIBUTIONS OF DR GOPALAN

Bhat R V

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## Introduction

Dr Gopalan, in his early career as an original researcher during the late Fifties and early Sixties, devoted considerable time to research relating to food toxins, and the burning problems of the time: lathyrism and the newly discovered aflatoxins. Dr Gopalan visited the place where lathyrism was a scourge, namely, the Chak ghat area on the banks of the river Tamasa in Rewa district of Madhya Pradesh. He carried out field studies, and interacted both with the victims of paralysis as well as with the local public health officials. Dr. Gopalan was convinced that the consumption of lathyrus as a staple was the main cause of the outbreak of lathyrism. He was instrumental, as far back as in 1961, in urging a ban on the sale of the kesari dal (*Lathyrus sativus*) as a public health measure under the Prevention of Food Adulteration Act. The ban on the sale of the pulse that was initiated by the Government of India then, is in vogue in many of the States even today. As Director of the then Nutrition Research Laboratories, he recruited a band of dedicated workers such as Dr V.Nagarajan and Dr D N Roy to work on the problem. Dr Gopalan's group was responsible for the first major breakthrough in experimental studies on lathyrism a breakthrough that had been eluding the then Nutrition Research Laboratories for over three decades. His group, using a simple experiment of injecting alcoholic extract of *Lathyrus sativus*, demonstrated the toxicity in day old chicks<sup>1</sup>. This experiment was the basis for the discovery by the Nutrition Research Laboratory of the active toxic principle, an unusual amino acid, beta oxalyl amino alanine, and of diamino propionic acid by the Indian Institute of Science group, which was headed by the eminent biochemist Prof P S Sarma. Dr.Gopalan also encouraged research into initiating preventive measures such as detoxification of the pulse through simple household methods of boiling and discarding the boiled water. Because of his abiding interest in the subject of lathyrism, Dr Gopalan revisited the lathyrus cultivation and consumption area of Rewa district after 25 years in 1983. He published the findings in the Second Report of the Nutrition Foundation of India. "The Lathyrus Problem: Current situation and new dimensions"<sup>2</sup>. Again, after a further 25 years, in 2008, during a Symposium on National Nutrition Policy held at the NFI, he recalled his earlier visits to Rewa and expressed the satisfaction that at least the acute effect of lathyrus toxicity in the form of human paralysis is now history. Also, he found evidence for the pulse being sent to other States in the country and used as an adulterant<sup>2</sup>. This chronology of events of the work of Dr Gopalan on lathyrism should set at rest the meaningless insinuation attributed to Dr Kothari in the article "out of pulse" in the 16-30, 2008 issue of the periodical Down to Earth<sup>3</sup>.

Aflatoxins, the toxic metabolite of the fungi *Aspergillus flavus* and *A. parasiticus*, were discovered in the UK in 1961 consequent to the death of

more than one lakh turkey poults. The toxin was traced to the feed ingredient of groundnut meal imported from Brazil. India was one of the major groundnut producers in the world and had a large export trade in groundnut meal. Dr. Gopalan initiated research into the occurrence and biological effects of aflatoxins in experimental animals, with a dedicated team of workers including a biochemist, Dr P G Tulpule, and a pathologist, Dr Madhavan. Within a couple of years of the discovery of aflatoxins, Dr Gopalan's group fed large doses of aflatoxins to rhesus monkeys and found that they developed hepatic cirrhosis within four weeks, thus demonstrating the harmful effects of aflatoxins in primates for the first time<sup>4</sup>. The team was also the first to indicate that animals that are protein-deficient are much more susceptible to aflatoxins than well-nourished animals<sup>5</sup>. Also, his group was the first to demonstrate the carcinogenic effect of aflatoxin in monkeys. He took a leading part in the then Protein Advisory Group of the UN, highlighting the global nature of the problem.

The philosophy Dr Gopalan believed in was that the “major objective of research programmes is to identify important problems, to understand the factors underlying their causation and development”, be they nutritional or problems of food toxins, “and to discover the most effective and practical methods for their prevention and control”. The achievement of such an objective implied close integration of the research programme in the laboratory, field and clinic. According to him, the laboratory should function as a single unit and not as a conglomerate of several autonomous divisions, each pursuing its own independent research programmes<sup>6</sup>.

The first-hand experience of food toxins and his great attachment to public health, prompted Dr Gopalan to shift emphasis from food toxins to food safety in the interests of the consumers. He strongly believed that any new technology, be it food irradiation in the seventies or the present day “untested and unproven newer technologies” such as genetically modified foods or nano-technology need to be thoroughly investigated to ensure that they do not pose any danger, short-term or long-term, to human health. The officials of the Department of Atomic Energy in the seventies were in a great hurry to push newer technologies. Dr Gopalan was advocating great caution in permitting the use of irradiated wheat for daily consumption, based on the scientific findings published in peer-reviewed journals. Though the use of irradiated technology was ultimately cleared by the Government of India, its limited use even today, after three decades, in mass consumption items like wheat, is a testimony to the vision of Dr. Gopalan.

### **Building of infrastructures for food safety research**

Realising the importance of the issue of food toxins and food safety, Dr Gopalan was instrumental in establishing the Food and Drug Toxicology Research Centre at Hyderabad as an independent institution of the Indian Council of Medical Research. When he was appointed as the Director General of Indian Council of Medical Research, he further strengthened the research on food toxins and food safety by establishing the joint ICMR- ICAR panels for collaborative research. He also encouraged investigations into

food-borne disease outbreaks in different parts of the country. The scientists of the National Institute of Nutrition investigated the outbreak of toxic hepatitis in parts of Rajasthan and Gujarat in which over 100 persons died. The cause of these deaths was traced to the consumption of maize heavily contaminated with aflatoxins. This first-ever report in 1975 was followed by a report of a similar outbreak in Kenya during 1982, but these reports did not get the attention of the world, the more recent outbreak of aflatoxic hepatitis in Kenya during 2004 and 2005, investigated jointly by the Government agencies of the USA such as FDA, CDC and USDA, had unequivocally confirmed the pioneering work done in India. The prophecy made by Dr Gopalan and Dr Tulpule way back in the mid-sixties after demonstrating the harmful effects of aflatoxins in primates that “although there have been no reports of human poisoning by these compounds, these findings in primates are suggestive of the possible harmful effects of aflatoxin to man”, were confirmed thirty years later!<sup>7,8</sup> .

The investigations of endemic ascites resulting in the death of 70 persons in Sarguja district of Madhya Pradesh was shown to be due to venoocclusive disease due to consumption of staple millet contaminated with weed seeds of *Crotalaria*. The controversy it evoked in the popular press and its handling was a tribute to Dr Gopalan’s administrative acumen. It was Dr. Gopalan’s vision of building the necessary infrastructure, laboratories and human resources that helped in identifying and solving the public health problems and in securing a firm place for India in the international area of food safety research<sup>9</sup> .

### **Emphasis on policies and programmes on food safety**

Dr Gopalan stated that developing societies are particularly vulnerable, because they do not have adequate safeguards to ensure the safety of foods. Quite often, the health effects of food contamination can be insidious and may even escape diagnosis. Lack of food safety could also entail a heavy economic loss to the country through rejection of its exports. Unfortunately, the importance of ensuring food safety is not widely recognized. The current policies and programmes for ensuring food safety are wholly inadequate and require to be considerably strengthened. For this reason, in the year 2003, Dr Gopalan, under the auspices of the Nutrition Foundation of India, organized a Workshop on National Strategy to Ensure Food Safety, involving multisectoral and multi disciplinary group of experts in the area of food safety. After discussing various facets of the problem of food safety, the workshop arrived at practical and concrete recommendations for strengthening the infrastructure for ensuring food safety. The recommendations of the workshop have indeed helped the Government of India to address the problems of food safety in an integrated and comprehensive manner, in order to ensure that the standards of food quality in India compare favourably with global standards and to bring about greater confidence in the safety of our food supply, in both domestic and foreign consumers. These recommendations were also of great interest to the food industry and to the consumers who play major roles in the production and consumption of safe wholesome food<sup>10</sup> .

The Government of India introduced the Food Safety and Standards Bill in Parliament in 2005 to consolidate the laws relating to food, and to establish the Food Safety and Standards Authority of India for laying down science-based standards for articles of food and to regulate their manufacture, storage, distribution, sale and import, to ensure availability of safe and wholesome food for human consumption and for matters connected therewith or incidental thereto. Though the bill is yet to be fully implemented, and the teething troubles of operationalising the Food Safety and Standards Authority are yet to be overcome, the beginning made will no doubt soon lead to its logical conclusion.

### **Highlighting unfinished tasks**

Dr Gopalan has always believed that, although the gains of the past have been impressive, a great deal needs to be done before the problems of poverty and malnutrition are fully eliminated, not only in India and South East Asia, but also from the whole of Asia. He was for looking at the problem of food safety not in isolation but in the context of the entire gamut of development activities, in a multidimensional perspective. He considers that the essential components necessary for solving the problem of food safety, quality and hygiene are: increased production and the availability of good quality foods (especially of important foods such as pulses, horticulture produce, milk, etc), ensuring adequate access to food, anti-poverty programmes, aggressive spread of education, especially female education, and income generating skills as.

The factors influencing future development are bound to have profound influence on the nutrition scene. These include urbanization, information technology revolution and globalization. Dr Gopalan is a strong advocate of homegrown solutions rather than accepting the “western models” as perfect. He has been and still is urging Asian countries to seek to foster and cherish traditional practices that have been proved to be conducive to general health and well being. At the same time one should be receptive to new ideas and new technologies of proven value and safety for combating the entire gamut of problems of nutrition including those relating to food safety, quality and hygiene<sup>11</sup>.

It is hoped that the concerns expressed by Dr Gopalan about the various consequences of the lack of food safety and his repeated emphasis on the steps that need to be taken to improve the scenario in terms of infrastructure requirements, policies, corrective measures, education and extension activities, will ensure the availability of safe, hygienic and good quality food both for domestic consumption and for export.

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# CALL FOR A NEW MINISTRY OF HEALTH, NUTRITION AND POPULATION

**Bose A**

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*Dr. C. Gopalan is undoubtedly the Nutrition Guru of India, having devoted a lifetime to research and imparting training in nutrition, and having inspired numerous scholars in India and abroad. I fondly recall my first meeting with Dr. Gopalan at a conference in Delhi several decades ago. I was overwhelmed by his personality, his dignified demeanor, clarity of presentation and genial manners. The United Nations had declared 1974 as the World Population Year and convened a World Population Conference that year. On behalf of the Indian Association for the Study of Population (IASP), I was involved, along with some of my colleagues, in bringing out a book on Population in India's Development as our modest contribution in the World Population Year. This volume, published in 1974, comprised 36 contributions from scholars belonging to a whole range of disciplines. We requested Dr. Gopalan (then Director General, Indian Council of Medical Research) to contribute to the volume, and he agreed readily. He had a modest caption to his paper – "Some Aspects of Nutrition in India". His foresight in putting nutrition centre stage will be evident from the concluding sentence of his paper: "A comprehensive nutrition programme, therefore, should not only aim at improvement of the diet but also at improvement of the environment, control of infections, nutrition education, health education and family planning. An integrated programme including such mutually reinforcing components will be the most rewarding strategy to be employed for the conquest of malnutrition in our country."<sup>1</sup> The rewarding strategy suggested by Dr. Gopalan has not been operationalised. There is no worthwhile national nutrition programme in India. This paper argues that nutrition must be put centre stage and it would be best if the Ministry of Health and Family Welfare, both at the Centre and States, is reorganized and called Ministry of Health, Nutrition and Family Welfare.*

## **Introduction**

In 1983, IASP was privileged to have Dr. Gopalan deliver the inaugural address at its annual conference. In his address, Dr. Gopalan highlighted the vital importance of nutrition for adolescent girls. In my book "From Population to People" (1988), I reproduced Dr. Gopalan's article "Combating under-nutrition: basic issues and practical approaches" published by the Nutrition Foundation of India (NFI), in which he proposed the establishment of special schools for arts and crafts in villages, exclusively for girls between the ages of 12 and 20 years. He enumerated the suggested topics for practical training of these girls, including "Nutrition: the value of different local foods and the types of nutritious recipes that can be fashioned out of them, preparation of inexpensive diets out of foods available in the village"<sup>2</sup>. He argued that "the most crucial segments of our population from the point of view of the quality of our future generation are today's young girls who are just on the threshold of marriage and motherhood. These girls are future homemakers"<sup>3</sup>.

Nutritional Parameter	NFHS-1 (1992–93)	NFHS-2 (1998–99)	NFHS-3 (2005–06)
Stunted	52.0	45.5	38.4
Wasted	17.5	15.5	19.1
Underweight	53.4	47.0	45.9
Note: Figures of NFHS-1 above are for 0–4 years. However, NFHS-1 later generated data for below 3 years children with 51.5% children being underweight.			
Source: NFHS surveys, IIPS, MoHFW, GoI.			

In spite of the completion of ten Five-Year Plans, and with the Eleventh Five-Year Plan (2007-2012) currently under way, there has been no perceptible improvement in the nutritional status of our poor populations. The situation is particularly distressing in the case of women and children, as

revealed by numerous surveys such as National Sample Surveys (NSS), District Level Household Surveys on Reproductive and Child Health (DLHS) and National Family Health Surveys (NFHS). The Eleventh Five Year Plan does refer to the disturbing trend in malnutrition in children, as revealed in data from three rounds of NFHS (Table 1).

The Planning Commission does not hesitate to point out that, after comparing data for underweight children in NFHS-2 (1998-99) and NFHS-3 (2005-06), one notices “hardly any change over a period in which the economy has been growing at over 6% p.a. on average”.<sup>4</sup> The 11<sup>th</sup> Five Year Plan also quotes NSS data to observe that “overall per capita intake of calories and protein has declined consistently over a 20-year period from 1983 to 2004-05”.<sup>5</sup> Table 2 gives the details:

	Calorie		Protein	
	(k cal/day)		(g/day)	
	Rural	Urban	Rural	Urban
1983 (NSS 38 <sup>th</sup> Round)	2221	2089	62.0	57.0
1993–94 (NSS 50 <sup>th</sup> Round)	2153	2071	60.2	57.2
1999–2000 (NSS 55 <sup>th</sup> Round)	2149	2156	59.1	58.5
2004–05 (NSS 61 <sup>st</sup> Round)	2047	2020	57.0	57.0
Source: NSS Report No. 513, Nutritional Intake in India, 2004–05.				

NFHS-3 data show that anaemia among children and women is on the rise. For example, according to NFHS-2, 74.2 % of children (6-32 months) were anaemic. The comparable figure in NFHS-3 was 79.2 %, showing a distinct rise in anaemia in children. Similarly, the percentage of anaemic married women in the age group 15 - 49 years has increased from 51.8 % (NFHS-2) to 56.2 % (NFHS-3), again a distinct rise. In the case of pregnant women (15 - 49 years), the rise was striking: from 49.7 % in 1998-99 to 57.9 % in 2005-06.<sup>6</sup> All in all, the picture on the nutrition front is very depressing. The government has launched several schemes from time to time, to improve the nutritional status of women and children. Against the background of these efforts, the worsening status of nutrition must make us sit up. What has gone wrong? Are the well-meaning schemes not properly implemented? Have we failed to spread nutrition education? Have we allocated inadequate funds for nutrition programmes? Have we paid only lip service to nutrition?

In this context, it may be noted that, over the years, the nutrition portfolio has shifted from one Ministry to another. At one time it was under the Ministry of

Rural Development, and was later shifted to the Ministry of Human Resource Development. Currently it is under the Ministry of Women and Child Development. The ICDS programme is overseen by this Ministry. However, programmes such as National Iodine Deficiency Disorders Control Programme, and National Programme for Control of Blindness, are under the Ministry of Health and Family Welfare.

It is time for us to move to an integrated Ministry of Health, Nutrition and Family Welfare, which will take an overarching view of these three vital social sectors, which is exactly what Dr. Gopalan had pleaded for long ago. It is nobody's point that a mere change in nomenclature of the Ministry alone will improve things. It should be only the starting point in our agenda for improving the quality of life of millions of people, particularly women and children.

The DLHS surveys present nutrition data by “standard of living index”<sup>7</sup> in three categories: low, medium, and high. It is intriguing to note that the figures for anaemia among children (0-71 months) do not show any marked differences with age (Table 3).

<b>Table 3: Anaemia Among Children</b>				
Percentage of children (age 0-71 months) classified as having iron-deficiency anaemia by degree of anaemia and by selected background characteristics, India, 2002-04.				
Background characteristic	Percentage of children with any anaemia	Percentage of children with		
		Mild anaemia	Moderate anaemia	Severe anaemia
Age of child (in months)				
0-5	96.0	42.1	50.0	3.9
6-11	97.8	39.2	54.5	4.1
12-23	97.6	37.7	55.7	4.3
24-47	96.7	47.9	45.5	3.3
48-71	95.2	58.2	34.9	2.1
Source: DLHS-2, 2006				

It will be seen that the percentage of children with “any anaemia” is as high as 95.3 in the “high standard of living” category and 96.9 in the “low standard of living” category. The differences become somewhat sharp when one considers the different categories of anaemia – mild, moderate and severe. One may legitimately ask: why is there such a high incidence of “any anaemia” in the “high standard of living” category? Is it because of ignorance about nutrition? Surely, it cannot be poverty, which can explain this.

The NFHS reports have introduced the concept of “Wealth Index” based on the possession of a number of assets. The data are given for each of the five quintiles (20 % of the total). As an example, NFHS-2 gives data on the percentage of children (6-59 months) with anaemia, cross classified by Wealth Index (Table 4). One would have expected sharper differences in the anaemia figure when cross classified by Wealth Index. Do the parents of these children know anything about anaemia? Do the mothers, in particular, know what to feed children? How is it that in a prosperous state like Punjab the prevalence of severe anaemia (6.6 %) is the second highest in India, just marginally less than in Rajasthan (6.7 %) which shows the highest level of severe anaemia? These are indeed tricky questions. Unless one blames the

concepts, methodology of data collection and accuracy of the figures collected in NFHS-3, these tricky questions have to be answered. It may be mentioned that the analysis of anaemia estimates is restricted to the last two children of ages 6-35 months of ever-married women who were interviewed for the survey. The NFHS-3 report concludes that “the prevalence of anaemia increased from 74 % in NFHS-2 to 79 % in NFHS-3. The increase is seen primarily in rural areas, where anaemia rose from 75 % to 81 %”<sup>8</sup>.

Wealth Index	Mild	Moderate	Severe	Any Anaemia
Lowest	27.7	45.8	3.0	76.4
Second	26.9	43.4	3.3	73.6
Middle	26.2	39.7	3.4	69.3
Fourth	24.9	37.3	2.6	64.8
Highest	25.0	29.2	2.1	56.2
INDIA	26.3	40.2	2.9	69.5

Source: NFHS-3, 2006-07

There is a Nutrition Cell in the Directorate General of Health Services to coordinate programmes such as Control of Micronutrient Deficiencies, which is being implemented by All India Institute of Hygiene and Public Health, Kolkata. There are also programmes such as Double Fortification of Salt (DFS), Prevention and Control of Fluorosis, etc. In our view, the vital importance of nutrition demands much more activity than those currently undertaken by the Nutrition Cell. The National Rural Health Mission (NRHM) launched by the Prime Minister in 2005 is an ambitious programme for upgrading rural health. Under the umbrella of NRHM, there should be a significant increase in funding for nutrition programmes.

The shockingly high rural infant mortality rates reflect the high degree of undernutrition and malnutrition in our villages. According to the latest SRS data, in 2006 the IMR in rural Madhya Pradesh was 79 per thousand; in Orissa it was 76 per thousand, in Uttar Pradesh the figure was 75, in Rajasthan 74, in Assam 70 and in Bihar 62 per thousand<sup>9</sup>. All these States are designated as “high focus” States in NRHM<sup>10</sup>, targeted to receive priority. If there is no marked improvement in the nutritional status of women and children, these high rates of IMR will persist. In this context, one must realise that much depends on the extent to which our anti-poverty programmes succeed. Rising inflation has added immensely to the misery of the poor and this will adversely impact the nutritional status of these poor households. In the face of these figures, no worthwhile programmes for human resource development make sense unless there is a strong input of nutrition, especially for women and children. The Nutrition Foundation of India (NFI), of which Dr. Gopalan is the President, has played a pioneering role in highlighting the importance of nutrition. The NFI will have to carry the flag of Dr. Gopalan further in the coming years. May the NFI receive personal guidance and inspiration from Dr. Gopalan for many more years!

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## **ETHICAL DILEMMAS IN CARRYING OUT CLINICAL TRIALS IN INDIA**

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*Dr. Gopalan's contribution to medical research cannot be adequately described. He has not only personally carried out research which is still being quoted today but he has thought, throughout his long and distinguished career, beyond the confines of the laboratory to the health needs of the country. He has been responsible not only for the development of some of the leading institutes in our country but also for creating a very large number of scientists who have also contributed to research and research development in India.*

*Dr. Gopalan always set the highest standards of functioning for himself and was an example to his colleagues and students. His ability to gauge the quality of persons, his instinctive ability to take the right decisions in as short a time as possible, his incisive brilliance in analysing situations and his vision in looking into the future were complemented by his empathy towards the younger scientists trying to find a foothold, and his unfailing help to those not as talented as himself.*

*During his tenure as Director of the National Institute of Nutrition he saw the need for developing clinical pharmacology and toxicology – areas which were not being thought about at that time. During his tenure as Director General of the Indian Council of Medical Research he saw the need for mechanisms such as the Toxicology Review Panel, the Ethics Committees and the creation of a number of Task Forces in Human Reproduction. Many of these activities became possible only because Dr. Gopalan laid down the thinking and the foundations. I have mentioned only those areas in which I was and am personally involved; there would be many other areas where similar imprints of Dr. Gopalan would be seen today. It is a privilege to contribute to the Festschrift being brought out on the occasion of the ninetieth birthday of Dr. Gopalan.*

*I have chosen to write on a subject which is of growing importance to our country. It is also an area in which the expertise and institutions developed by Dr. Gopalan are playing a leading role. These are in clinical pharmacology, toxicology and ethics of clinical research. These institutions are enabling us today to regulate and benefit, in an ethical manner, from carrying out more and more national and international clinical trials in India. These are the areas Dr. Gopalan thought about at a time when nobody else in the country did.*

## Introduction

India has become an international centre for clinical trials for new drugs being developed both in India and abroad. The reasons for carrying out clinical trials are many:

- genetic diversity of the population
- a large variety of diseases
- a large drug-naïve population
- 272 medical colleges throughout the country
- competent clinicians throughout the country having fluency in English, and
- the relatively low costs of carrying out clinical trials in India – sometimes as much as 1/10 the cost of carrying out similar trials in countries in Europe and in the USA.

One needs to recognise that there are both potential benefits and potential hazards to our country becoming a hub for clinical trials. The benefits are:

- participation by Indian researchers and clinicians in the frontier areas of drug development
- providing a platform for carrying out clinical trials of drugs developed in India
- creating expertise in areas such as clinical pharmacology and clinical toxicology and in carrying out Phase I studies in India
- increasing job opportunities on an immense scale for Indian scientists and clinicians and their back-up staff
- bringing resources into the country. It has been calculated that, by 2015, investments relating to clinical trials in India would be 2.2 billion US dollars

However, there are many dangers and hazards in our endeavour to become an international centre for clinical trials. These are:

- carrying out clinical trials in any of our hospitals or medical centres which have not been approved by the drug regulatory authority, or carrying out unethical clinical trials
- exploiting our people, particularly the illiterate and the poor and carrying out clinical trials on them by giving them some financial incentive
- carrying out badly planned clinical trials which are scientifically unacceptable, making these trials a useless exercise

It is for the scientists, policy makers, drug regulatory authorities and clinicians to ensure that this country benefits from the increasing number of clinical trials without exposing our population to unnecessary risk, and without exploitation. This is the challenge before us. The Indian Council of Medical Research has been the leading organization, which has thought far ahead and has taken a series of remarkably visionary steps in developing both the facilities for clinical trials in India and the mechanisms and safeguards to ensure that the people will not be exploited.

## **Steps taken by ICMR to prevent misuse of clinical trials**

Some of the steps the ICMR has taken in setting up mechanisms to prevent misuse are:

- development of Ethical Guidelines for Clinical Trials and clinical research in the country, and wide dissemination of these guidelines
- establishment of a Toxicology Review Panel
- development of Institutional Ethics Committees all over the country
- setting up a good system for review of proposals for clinical trials

There are many other steps the ICMR has taken to try to prevent unregulated, unscientific and unethical trials from being carried out in the country. I have been fortunate to work with the ICMR in setting up some of these mechanisms, and the tremendous contributions of the ICMR staff throughout the last thirty years in this endeavour needs to be recorded.

On a parallel track, the Council has, in the last twenty years, been developing a number of Advanced Centres in specialized areas related to clinical trials all over the country so that when, as now, the demand for more clinical trials in India arises, we are prepared to meet it. Several of these advanced centres are important for detecting possible toxicity of the drugs going into trials immunotoxicity, reproductive toxicity and genotoxicity centres. The National Institute of Nutrition at Hyderabad is today a leading international centre for carrying out pre-clinical toxicity studies in animals – a facility that was sorely lacking in India. These centres, over thirty five in number in specialised areas of clinical trials, are scattered all over India. The role played by the Indian Council of Medical Research in placing India in the forefront of clinical trials research in the world and also in safeguarding against misuse of clinical trials remains to be recognized, and I believe this Festschrift in honour one of the most distinguished Directors General of the Indian Council of Medical Research, Dr. Gopalan is the proper place to bring this out.

Carrying out ethical clinical trials which would bring in resources without exposing our patients and population to unjustified risks, preventing exploitation of our poor and illiterate population and yet keeping us on the front-line areas of clinical research, are major challenges. These challenges are compounded by the fact that we are a vast country with an enormous population, much of it below the poverty line, and that we have a system wherein state governments share the responsibility for health services.

These factors pose many dilemmas which are specific to us and we need to resolve these problems in our own way as there are no readily available models elsewhere. It has been my good fortune to deal with some of these issues as Chairman of the Ethics Committees of the Sir Ganga Ram Hospital, the Indraprastha Apollo Hospital and the International Centre for Genetic Engineering and Biotechnology, and in my capacity as a member of the Central ICMR Ethics Committee. It is this experience that I bring to the reader in this manuscript, and I shall describe only a few of the many dilemmas.



## **Cardinal principles for clinical trials**

The four cardinal principles of medical ethics that need to be strictly followed in the conduct of clinical trials are:

- Autonomy – freedom of choice;
- Non-maleficence – not doing harm;
- Beneficence – doing good; and
- Justice – equal allocation of resources

It is against this backdrop that I shall discuss a few of the dilemmas facing us in India. These are:

- Informed consent
- Patient rights – the patient
- Use of the placebo
- Ownership of data

### ***Informed consent***

I was privileged to prepare the draft of the Ethical Guidelines of the ICMR in 1980, and again took part in the development of the Guidelines prepared in 2005. As a result I had extensive discussions both with the late Justice Khanna and with Justice Venkatachaliah on this issue. It is very clear that obtaining truly “Informed” Consent from the participants of a trial in a largely illiterate and poor population is not easy. There are three important steps in the process of obtaining Informed Consent. These are:

- Information about the trial to be given to the patient
- Understanding of this information by the patient
- Consent by the patient to participate in the trial after understanding the information provided

### ***Information about the trial***

The Patient Information Sheets which provides information about the drug to be evaluated and the trial are, in most cases, quite inappropriate for our population. Nearly always, for multicentre trials, these sheets are developed in the USA, Europe or the UK, and consist of 20-25 pages of information much of which uses technical jargon that will not be understood by the patient. Very often the translation into Hindi is so stylized that very often this is not understood even by the physician. There is no readable, reader-friendly summary provided. The pharmaceutical companies are not agreeable to changing the Patient Information Sheet because it will have to be used uniformly in all the participating countries around the world. Herein lies the dilemma.

### ***Understanding by the patient of the information provided***

Very often the patient or the volunteer does not understand or comprehend what is being said or what the implications are. By and large the patient still

has full trust and confidence in the doctor, and if he understands that the doctor wants him to participate in the trial he is very willing to do so.

### ***Consent by the patient after understanding the information***

Because of these reasons, consent to participating in the trial will, in many instances, not be a truly “informed” consent, although a signature is usually sufficient proof of having obtained Informed Consent.

Although it is not easy to obtain truly Informed Consent, the following suggestions may be considered:

- Just as the US FDA and the multinational pharmaceutical houses insist on a detailed Patient Information Sheet, the office of the Drugs Controller General of India and the Ethics Committees in India should insist also on a 2-3 page Patient Information Sheet summary which, in simple language, tells the patient what he or she should know about the drug and the trial proposal. The translation should also be easy to understand.
- An independent person appointed by the Institutional Ethics Committee should be present when the information is presented and should certify that the patient has understood the information that is being provided.
- This same person should certify that the patient agrees to participate in the trial. The actual consent could be written consent as is obtained now or even verbal consent made in the presence of this person or other members of the community.

### **Patient rights**

There are several issues relating to patient rights and national benefit which are specific to a country with poor populations. Some of these are described here.

### ***Use in the country after approval***

Since the patients and volunteers in a clinical trial have actually contributed to the data which eventually may lead to the approval of the drug for marketing, it would not be ethical if the drug is marketed only in the affluent countries and not in India merely because the profit margins may be meagre. This has happened in the past. The suggestion made here is that the Drugs Controller General, when approving clinical trials for a new compound, should insist on an undertaking from the pharmaceutical house that if the drug is eventually approved and marketed it would be released in India also at a price that is reasonable. This is reasonable because the Indian studies would have contributed to the release of the drug.

### ***Vulnerability of patients in a trial***

Many patients and volunteers participate in clinical trials because of the money paid to them. In addition, there will be other benefits in joining the trial e.g. health care to the family, free medicines at the hospital and free

diagnostic tests. This runs counter to the cardinal principle of *autonomy* mentioned earlier in this paper. I do not know if we are violating the principle of autonomy by providing free drugs and treatment. Is the choice the patient makes truly a free choice? In an earlier paper<sup>1</sup> I have clearly stated that patients should not be compelled or unfairly enticed to participate in a clinical trial. The challenge for researchers is to establish procedures that are ethically sound and culturally sensitive and to bring in community involvement in clinical trials research.

### ***Patients enrolled in clinical trials when trials are closed***

Pharmaceutical houses plan their international multicentred clinical trials on the assumption that a certain number of patients will be recruited and that a certain number will complete the trial. It has happened in the past that just when a trial gets going in India, these numbers are completed because of recruitment of patients in other countries. The trial is then stopped in India. It is important to ensure that all persons in the trial receive their drugs for the entire length of time which was originally proposed. This should be a built-in safeguard when approving a clinical trial. In a protocol for a drug to be administered to a HIV-positive mother just before delivery and immediately after – to prevent the baby from becoming HIV-positive it was proposed that the drug to the mother would stop at the end of the trial. This would have meant certain death for the mother. On the request of the ICMR Ethics Committee the pharmaceutical house agreed to provide the drug free of cost, for life, to the mothers who had participated in the trial.

### ***Access to drugs***

Even if a drug is released after clinical trials in India, the participants in the clinical trial may not be in a position to purchase the drug because they cannot afford the cost. Patients who participated in the trial and whose data helped to obtain clearance for the drug to enter the market should be able to obtain those drugs throughout their life at a reduced price or entirely free.

### ***Information***

No information is ever provided about the outcome of the trial to the patients who participated in the trial. As partners in drug development in India in the 21<sup>st</sup> Century such information, when released, should be provided not only to the participants of the trials but also to the community.

### ***Use of the placebo***

Hardly any meeting of any Institute Ethics Committee takes place without a discussion on the ethics of using a placebo or dummy tablet in one group of patients in that particular trial. There is a difference of approach between the United States Food and Drug Administration and the Indian Drug Regulatory Authority and the Indian Council of Medical Research. According to the U.S. FDA regulation, the first Phase II clinical trial of a new drug must be an evaluation of the efficacy of the new drug against the effects of a group of

patients on placebo. They feel that this trial is essential to determine the efficacy of the new drug. Our approach in India is that it is unethical to give a placebo to a group of patients when there is a drug available to cure that disease. We believe that the first trial should be to determine the comparative efficacy of the drug against the existing drug. This is the stand taken by the Toxicology Review Panel of the ICMR, which I have chaired now for over twenty years. The most recent ICMR Ethical Guidelines, brought out in 2007, clearly states that there is no role for a placebo in assessing the efficacy of a new drug in conditions for which there is already an effective drug.

One condition wherein the use of a placebo is often discussed is the evaluation of new drugs for diabetes. In a typical multi-centred trial developed in the USA, patients with mild to moderate diabetes will have to first stop their existing treatment regimens and could then be allocated to either of two groups – the placebo or the new drug. In this design it is possible that a diabetic patient who is stable on an anti-diabetic drug would be taken off the drug and could be assigned to the placebo or “no drug” group. We consider this to be unacceptable and unethical, and a trial with this design will not be approved. There are therefore many dilemmas. The suggested solution to resolve dilemmas of this type is to try and harmonize the guidelines between countries. That will go a long way in removing certain glaring differences, although some differences in approach will always remain.

### **Clinical evaluation of traditional medicines**

The clinical evaluation of traditional medicines and medicinal plants presents several unique ethical dilemmas that are not being discussed here. Readers are referred to a chapter entitled “Clinical Trial Methodology” by Ranjit Roy Chaudhury, Urmila Thatte and I. Liu in the book published by the Imperial College, London last year.<sup>2</sup>

### **Ownership of data**

The last controversial issue I want to discuss in this paper is the ownership of the data that results from the clinical trial. Who owns this data? Is it the drug company sponsoring the study, the Clinical Research Organization organizing the trial, the Chief Investigator of the project, or the institute, which allows the clinical trial to be carried out on the patients who come to the hospital? If a serious side-effect is encountered, who has to give permission for information about this side-effect to be published and widely disseminated? At the moment I believe that the ownership is with the sponsor of the trial and nothing can be published without their approval. What is needed is a dialogue on this issue by all players before a clinical trial is initiated. There should be a clear understanding that if a serious side-effect occurs the investigator will have the right, in fact the responsibility, to describe this occurrence at medical meetings and also publish the findings. The National Drug Regulatory Authority should ensure that this practice is followed.

At this juncture in the development of India’s booming drug industry, the increase in the number of patients coming to India from all over the world to

seek treatment, and the upsurge of clinical trials in India, we need to take a close look at the ethics of clinical trials and the ethical dilemmas we face. I am glad these are discussed in this Festschrift for Dr. Gopalan. Given his uncompromising stance on quality, efficiency, transparency and ethics there could be no better forum to present and share some of the dilemmas which face us and which we will resolve with guidance from medical “giants” like Dr. Gopalan.

### **Acknowledgement**

I would like to express my grateful thanks to the very large number of ICMR staff for their unfailing help and kindness to me over the last fifty years.

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## FOODS FADS, FACTS AND AMBIGUITY

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*It is truly a great privilege to have been invited to contribute to the Festschrift for Dr. Gopalan on the occasion of his completing 90 years of age. I met him first in 1964 at the National Institute of Nutrition, Hyderabad, during a seminar. I now meet him every time I go to Delhi. He is evergreen and a true scientist. He has countered effects of ageing with functional alertness and creative activity. He is one who authoritatively talks of the benefits of good nutrition in enhancing the body's resistance to infections, degenerative diseases and cancer; and its ability to withstand the toxic effects of pollutants. He still continues to contribute his proposals and comments in the Bulletin of the Nutrition Foundation of India, and critically reviews important issues of the status of public nutrition in India. How great! Salutations to him for his contributions!*

### Introduction

Every form of life needs nutrition for survival. Naturally, during the process of evolution of life, the potential sources and process of nourishment got transcribed on the genes. The choice of nutrients is genetically determined. While the nutrients for plants are inorganic, animals depend largely on organic nutrients for energy and growth. Herbivorous and carnivorous animals feed on grass and on meat, respectively. The mothers, when rearing their young, give practical training about food to their offspring. Humans are no exception. While the human being is basically frugivorous, grass cannot be digested, but meat can. Nutrients are obtained through food, which is available in the environment. Over the million and a half years of their existence on this planet, human beings have encountered the extremes of environment and habitat from the Equator to the Poles, and from season to season. During this long period, primitive Man explored and exploited Nature. Instinct led to a realization of the complex relationship between foods, diet and nutrition.

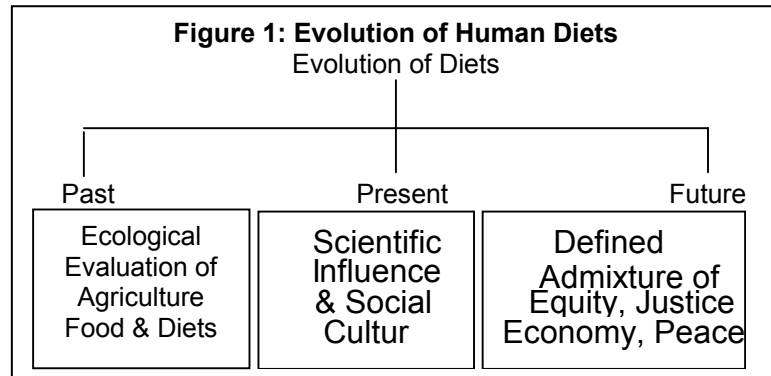
By using imagination and unbounded intelligence, by trial and error, and by critical evaluation, Man could select the right type of foods. Different locally available foods were carefully tested. Recognizing that no single foodstuff would result in proper nutrition, many foods were combined in sufficient quantity and proper proportions. Thus, ancient Man discovered and evolved diets to get all the necessary items required for proper nourishment of the body. Ecological interrelationship between plants and animals is reflected in the formation of the 'food-chain'. Man is a unit of the ecosystem and harbours millions of symbiotic microbes. 'Human Microbiome Project' of the National Institutes of Health, USA, suggests that, while human genes in the human body are 18,000 to 20,000 in number, microbial genes, over 3 million, are added on. What does that imply? Benefits?

The body's genetic structure interacts with the environment and adjusts itself. Thus, physiological and metabolic adaptations take place. By virtue of such

mechanisms, local foods could be digested and assimilated by the opening or closing of appropriate metabolic pathways. Thus, Eskimos near the North Pole derive their supply of B vitamins indigenously, probably from intestinal bacterial flora, while those living in the tropical areas get them also from green vegetables, etc. Hibernation is a biological mechanism enabling creatures to pass the winter or resting stage. In ancient times, ascetics are reported to have practised penance for long periods of time without eating any food. Did they acquire the ability to hibernate?

### Traditional wisdom

It is but natural that Man's 'foods' and 'diets' demonstrate socio-cultural and geographic variations. This successful adaptation to different ecological situations



on the earth was responsible for human survival even before the development of agriculture. Consequently, the variety of foods that is available to man is enormous. Another type of variation, which has been institutionalized by all societies, is manifested by different foods and courses for breakfast, lunch, dinner, snacks, and menus for festive occasions. Phases of dietetic evolution are shown in Figure 1.

In retrospect, the scientific soundness of the traditional Indian diets is amazing. The customary food combinations such as cereals plus pulses, and the staggering number of recipes, present the wonders of our cultural heritage. The inclusion of spices and condiments in the diet, probably because of awareness of their protective and medicinal usefulness, was a marvel. 'Curry-powders or Masalas' evolved with the culinary art. This should humble today's 'dieticians'. Most dietetic practices, food habits and other related traditions and customs, have stood the test of time. The importance of micronutrients, fibre, anti-oxidants and flavonoids has been recently emphasized, but even a cursory look reveals that several of our common foods are rich in them. About five decades ago, Sukhatme P.V. exploded the myth of 'protein gap' by proving that the problem was of 'food-gap'. In extending this further, nutrition security truly lies in our traditional foods and diets.

### Food fads

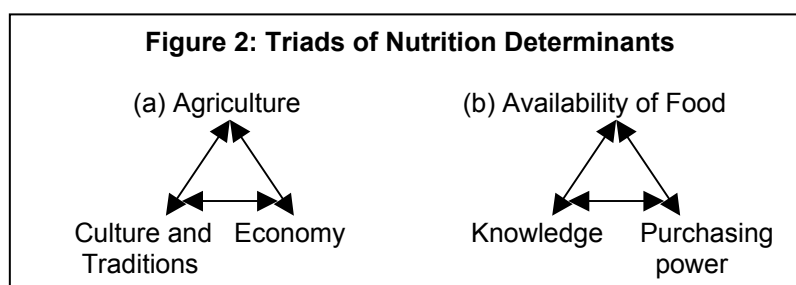
Because of ambiguity, fads associated with food are abundant. What to eat and what not to eat? Which foods are healthy and which foods can even harm? One man's food may be a deadly poison for another, as in the case of allergy or idiosyncrasy. Reader's Digest has published a book, "Foods that Harm and Foods that Heal" with a rider, "consult physician for specific health problem". Food fads such as '*excess of sweets cause diabetes*' are too many to list. There are contradictions, inconsistencies and vagueness. The social

and cultural dilemmas have become critical vis-à-vis new scientific knowledge on the nutritional value of foods. The reasons are: biological, ecological, historical, geographical, socio-cultural, commercial marketing of foods and globalization of trade.

## Public health nutrition

Human nutrition is in the phase of being under the influence of science and technology. In comparison to the cultural and conventional knowledge about food and nutrition, scientific and technological knowledge on nutrition is only about 250 years old and grossly incomplete. It lacks comprehensiveness. Ayurvedic concepts of nutrition and food cannot be ignored just because one fails to understand them, e.g., foods designated as 'cold' and 'hot', and incompatible foods: fruits and milk. There is need to recognize gaps in understanding and plan multi-disciplinary and integrated studies. Several scientific disciplines such as agriculture, economics, biochemistry, medicine, food technology, anthropology, health, epidemiology, etc., are concerned with some aspect of nutrition. The scientists tend to work in isolation. There is no common platform for collaboration and coordination.

The factors that determine human nutrition are shown in Figure 2. These are inter-related and variable at the family and community levels.



Nutrition security is of political and social concern. All the nutrition problems can be traced to one or more of these basic factors.

In public health, problems such as infestations like malaria, infections like tuberculosis, malnutrition like anaemia and low weight, etc., have rather simple solutions. However, determinants of disorders such as diabetes, coronary heart disease, obesity, hypertension and cancer are complex. Basic issues are insulin resistance, atherosclerosis, foetal malnutrition, unhealthy behaviour and life-styles. Unlike the developed countries and affluent societies, developing countries carry the double burden of infections and non-communicable diseases. Interventions such as primary health care, equity, behaviour change, reforms in life-styles, etc., are being badly managed. Poverty is the primary cause (and also effect) of emaciation and stunted growth, just as affluence is of obesity. There are globally new and emerging infections. What path should one take?

In the management of public health, one has to face difficulties in decision-making. The selection of effective interventions to control and prevent lathyrism is one such instance. What is best?

- to ban the cultivation and/or use of Kesari/Lakhi *dal*, or



- to educate people to limit the consumption of this *dal* to less than 25% of the total food, or
- to detoxify Lakhi dal by boiling or soaking it in hot water for some hours and throwing away the supernatant fluid?

Another example is of media sensationalizing the deaths of under/malnourished children, using terms like “hunger deaths”. Government and health departments respond by declaring nutritional interventions. However, the impact is never seen. While under-nourishment is the underlying cause of such deaths, the immediate cause of death is mostly respiratory or alimentary infection. These immediate causes are always ignored.

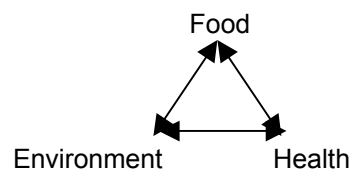
## Food hygiene

Food hygiene is a subject of concern to health authorities because of possible neglect and lapses by roadside vendors, eating houses and even the food industry. Are such foods safe? Are such food items prepared under hygienic conditions? Are good raw materials used? Are the chemicals added safe for health in the long run? Are the foods free of any contamination? One does not know. At the same time, some of the old family traditions provide us with examples of excellence of applied microbiology and asepsis in dietetics, e.g., the vanishing custom of observing *sovale* - type of isolation or sanctity, as a part of food hygiene. This custom originated unquestionably as an aseptic technique without the knowledge of which the surgical procedures such as reconstruction of the nose would never have been successful in ancient India. Old is gold. Traditions such as bathing and wearing self-washed clothes before cooking; not touching others while cooking, handling and serving food; discarding (contaminated) food from the servicing plate, if it is touched by someone other than the server are sound hygienic practices.

Personal hygiene is of great significance microbiologically. Washing of hands before eating food or after visiting the toilet is not just cleanliness, but a way of removing pathogenic microorganisms, and ova and cysts of helminthes. When one asks question such as, do you wash your hands clean? Everyone says ‘yes’ readily. But there is a gradation of cleanliness and one can see the manner in which hands are washed before taking meals and after eating oily food. Washing hands thoroughly is like using a clean spoon.

Human nutrition cannot be considered in isolation from the environment. Many dieticians tend to ignore this reality. Environment influences both food and health, and food intake determines health status (Figure 3). Physical environment can adversely or favourably influence human nutrition in many ways. The Indian Railways pollute the soil by directly depositing 51,000 to 71,500 metric tons of human faeces on the tracks every day. Important points that call for collaboration and cooperation of the agriculture, food, rural development, and other sectors are:

**Figure 3: Inter-relationship between Food, Environment and Health**



agricultural practices, variable requirements of nutrition, different dietary practices, contamination of food and water, Man being at the end of food chain, and the role of pests.

### **Research on nutrition**

In a consideration of public health practice and community nutrition, it is interesting to examine the contributions of scientific research on nutrition. The findings are:

- locally available foods should be used,
- a vegetarian diet can be as nourishing as a non-vegetarian one,
- a mixture of cereals and pulses, and variations in foods make diets nutritious, and
- breast milk is the best food for infants.

Apart from confirmation, have scientists really found anything new after spending time, effort and money to rediscover already known facts and practices?

Breast-feeding is widely prevalent in Bharat and even in India at a lower level. In our study, over 88 per cent of the infants were breast-fed and the others could not either because of poor milk secretion or illness of the mother. Lactation was generally prolonged, varying in duration from 6 months to 3½ years. About half of the mothers discarded the colostrum, while others fed it to the new born. Commercial propaganda on humanized milk and baby foods tends to discourage the breast-feeding practice. Branded baby foods are expensive and absolutely unnecessary. UNICEF and WHO (World Health Organization) have special programmes to popularize breast-feeding. Nature evolved mammals so as to ensure survival of the infants through breast-feeding! Nature's ingenuity is amazing in this regard; newborn has the inborn ability to search for the mother's nipple and feed itself. However, the irrational use of vitamins, glucose, proteins and protective foods, goes on unabated. Rationalization is still a distant dream.

Birth weight is an indicator of health of a baby. The gold standards for comparison are, however, unscientific. Since the recommended weight of 2,500 grams was based on 'formula fed' infants, WHO revised this to a lower scale. Still there are issues such as ethnicity. Is it right to expect birth weight of a newborn Naga to be the same as that of a newborn Punjabi? Gender difference in weights of male and female is obvious. It is strange; therefore, that cut-off weight at birth is the same for male and female newborn! Is it justified to label normal babies and children as under-weight or malnourished on the basis of an incorrect reference norm?

### **Shortcomings of current nutrition programmes in India**

Many activities are being undertaken in good faith, but without sufficient attention to their impact. ICDS has failed in ensuring proper growth and development of infants and toddlers. Despite decades of the National Programme for Prevention of Nutritional Anaemia, a majority of pregnant

women remain anaemic at the time of delivery. Paradoxically even with very poor management of vitamin A supplementation in young children, night blindness has virtually disappeared and xerosis is rare. Marasmus and Kwashiorkor are rarely encountered. The 2004 Atlas of the Sustainability of Food Security in India startlingly shows lack of relation between food security and poverty.

The outstanding feature of national nutrition programmes is lack of inter-sectoral coordination, collaboration and cooperation. The Rural Health Mission is under the Health Ministry; Integrated Child Development Services (ICDS) Programme is under the Ministry for Social Welfare; Grow More Food and fortification programmes are under the Food Ministry; Mid-day meal is with the Education Ministry; and the programme of Food for Work is with the Ministry for Rural Development. There are many management problems in timely and adequate supplies and storage facilities. Beneficiaries are selected according to the convenience of the staff, easy approachability, or influence. The needy, such as poor families, habitations that are difficult to access, preschool-age children and pregnant women are often not served. In mid-day meal programmes, the problem of substitution can be solved if the staple food is avoided as supplement. Popular snacks should be provided instead, as these are not be equated with a meal. There are many local recipes for snacks, and these should be used imaginatively. Feeding children at centralized locations has not solved the problem of malnutrition. It has several disadvantages such as risk of infection and food poisoning, inhibiting self-reliance, building an attitude of begging and helplessness, harming self-respect, and most of all, potential of inflicting psychological and cultural trauma on young children of tender age. In view of anthropological factors, it is desirable to consider a family as a unit for nutritional programmes, instead of targeting an individual as at present. This is also true for take-home foods, food for work and food subsidy. This will minimize, if not eliminate, the shortcomings listed earlier. Centralized programmes have many problems. There is no alternative to decentralizing feeding programmes.

### **Anthropological facets**

Sharing food is a cultural characteristic of India and cannot be ignored. Secondly, no single food can be universally suitable for all children between 6 months and 6 years. Food habits and tastes differ from family to family. When food is distributed at home, the variations for age, likes and dislikes, and habits are automatically taken care of. The women know the craft and there is no need to teach them recipes. It has also been shown that the sharing of food has no adverse effects in respect of malnourished children.

Many diets and items of food are associated with religious festivals and social functions. However, now they are available at all times. In Western societies decoration and style of serving food often get more attention than the food itself. In India, there is the *'thali'*, which integrates all the courses. The first serving indicates the menu. One can have second or more helpings. Foods are chosen based on the value system, the occasion, preferences and tradition. If one evaluates the meals poor people prepare on occasions such

as weddings, it is clear that they have a good concept of what constitutes a healthy and balanced diet. It is only that they cannot afford to eat such meals regularly.

The custom of religious fasting encourages consumption of foods other than the conventional ones. This kind of 'fasting' will not serve to prevent obesity. Our survey of middle-class families in Pune in 1962 revealed that, on an average, the consumption of calories and proteins was significantly higher on the day of 'fasting'. This was because of more consumption of milk and groundnuts than on other days. Given the status that food has in life, it is also used for cultural and religious purposes, e.g.,

- a lemon on a string of green chillies is tied to vehicles to ward off accidents;
- a cupful of tea is discarded by road-side stalls before service to the customers begin;
- rice grains, coloured or otherwise, are used during blessing at Hindu religious functions;
- food is offered to God by casting it in a flame; and
- a coconut is broken at auspicious events. When I see champagne being squirted around in celebration, I feel uneasy. Nonetheless, it is all a question of culture.

### **Commercial exploitation**

Vitamins such as vitamin C were discovered at a time when deprivation of food was extreme. Many vitamins were subsequently discovered. The discovery of the vitamins has, however, resulted in commercial exploitation rather than promotion of consumption of appropriate foods. Dr Gopalan had stated that the strategy of relying on massive doses of synthetic vitamin A for the control of night-blindness is inappropriate. Born out of recent studies on metabolism, new targets have become available for commercial exploitation, viz. fibre, anti-oxidants and bio-flavonoids. Their roles have been identified. The new term, "micronutrients", is frequently used. However, all these nutrients are adequately available in a wide variety of vegetables, fruits, and beverages such as black tea and wines. These form part of traditional diets. Unfortunately, these discoveries have provided new and sophisticated tools to the food industry for exploiting people. The consumption of preparations containing micronutrients, fibre, anti-oxidants and bio-flavonoids is on increase. Nevertheless, the rich don't need these and the poor need a balanced diet. An excess of anti-oxidants or fibre may even be harmful. Although the efficacy of vitamin E has not been established, its sale is rampant. Emphasis on the need to consume a balanced diet cannot be allowed to fade into the background. These new foods have benefited the manufacturers rather than the health seekers and patients.

### **Man-made scenario**

The basic problem of nutrition is Man himself. In the final analysis, politics and the power structure govern the food policy, production, distribution and pricing. Social and cultural factors are man-made and profoundly influence nutrition, choice of foods, feeding patterns, diets, etc. Examples include:

- cash crops verses cereals,
- irrigation, soil chemistry,
- storage & distribution of food,
- insanitary conditions and poor hygiene,
- choice of food vis-à-vis nutritional value,
- economics,
- commercial exploitation,
- mind-set and behaviour,
- adulteration,
- poverty,
- ignorance,
- brainwashing by media, and
- food supplementation

### **Modern era – progress or regression?**

In modern lifestyles, the choice of foods and eating behaviours has undergone a perceptible change (for the worse). Public nutrition has become topsy-turvy because of economic, occupational, social, migration-related, environmental, psychological and other reasons. Peculiar and extraordinary eating habits have become the order of the day. Eating habits are diversified and are influenced by taboos and customs, fads and fashions, religious teaching, scientific knowledge, likes and dislike, eccentric and idiosyncratic patterns, aggressive marketing of processed foods, the proliferation of restaurants, professional demands, health status, and other compulsions.

People eat fewer meals at home, and eating out is on the increase. The disadvantages of eating out are:

- overeating,
- the risk of eating mishandled, unsafe, inferior quality, or adulterated food,
- high intake of salt, sugar and fats; and
- gross reduction in the content of protective foods.

Apart from eating out, another curse of so-called modernization is a significant increase in the consumption of alcoholic drinks. The food industry, hotels and restaurants have come to stay. Many exotic foods are advertised. Attractively packed processed foods or ready-to-eat snacks or 'junk foods', baby foods, 'tonics', branded beverages, etc., have reached even remote places. Artificial sweeteners like Aspartame are present in many aerated soft drinks. These can cause metabolic acidosis. Long-term consumers of such drinks have suffered from muscle spasm and pain with illness resembling multiple sclerosis. Tonics are superfluous despite increased appetite due to alcohol they contain. Apart from exercise and yoga, some health clubs have started nutrition services for weight reduction and dietary care of diabetes and coronary heart disease. There is no quality control at many of these centres, and the services may not be scientifically correct.

Advances in science and technology often tend to make simple and cheaper things more complex and expensive. Attractively packed processed and

fortified foods charm customers. The sophisticated products such as 'ready-to-eat' are used by the privileged and unfortunately become status symbols. There is a tendency to follow the example set by the rich, and the limited financial resources of the underprivileged and poor are thereby wasted. Food adulteration is on the increase. Primary support for food adulteration comes from people who are eager to purchase food, which is cheaper than the market rate. When something is offered at an unreasonably low price, one should suspect adulteration or doubt the wholesomeness of the food. Food malls have started offering cheaper vegetables. Purchasing discounted food should be resisted because such food may not be wholesome or may contain adulterants. Whiter *dal*, pale peas and colourless sweets taste as good and are as nutritious as highly priced fortified commodities. Poverty level estimates should not be based on a single parameter such as expenditure on food. Empowerment, equity and social justice are at the root of poverty and malnourishment. Even basic needs such as food, shelter, employment and health are not available. There is a sense of urgency worldwide about the need to tackle these problems on a war footing.

## **Obesity**

Obesity and overweight are caused by excess intake of food (calories) over a long duration. By a rule of thumb, the weight of an individual at the age of 21 is his/her ideal weight. Extra weight gained thereafter, when active growth ceases, is due to fat deposits and is a signal that there is a need to control weight. Such weight gain is the earliest sign of health losing ground. Overweight or obesity is indicated by high BMI or high abdomen-to-hip ratio. It is good to aim for a BMI of 18.5 to 20. Weight-loss programmes are advertised claiming that 10 kg of weight can be lost in three weeks or even in 24 hours! This is unscientific and fraudulent. The rate of weight reduction should be slow, say one or two kg a month. This is possible by eating less caloric food, not eating out, brisk walking and exercise. Sure enough, some advise that one should 'fill the belly and reduce'. Many of those who lose weight regain it in about six months. Special care is needed to maintain the loss achieved. Some individuals are obese despite low food intake. The endocrine system may be at fault or there may be metabolic disorders. Drugs and surgery for obesity are not only of doubtful value, but may even be harmful. It is observed that many dietitians tend to prescribe diets *de novo*. Compliance with such diets is difficult and generally short-lived. Sooner or later one reverts to one's usual diet. This is why a majority of obese persons who were 'dieting' regain the lost weight within a period of six months or so, and diabetic persons are unable to control blood-sugar levels. It is easy and practical to modify one's customary/usual diet. Any drastic change cannot be sustained. In adult diabetics, there is need for demystification of the so-called 'diabetic diet' because it is just the usual food with some restrictions and modifications.

Tables giving composition of foods are used to estimate nutritional values of either raw or cooked food. However, there are pitfalls. Unless the limitations of such tables are clearly understood, the interpretations and the conclusions drawn may not be valid. The caloric needs of an individual may differ

markedly from the allowance recommended. In view of variations in water content, values for the proximate principles are more reliable than those for vegetables and fruits. Values for cereals and pulses are more reliable than those for vitamins and minerals. Nevertheless these tables are useful, if used and interpreted intelligently.

### **Self-reliance**

The best strategy is to eat traditional diets and wholesome food. The commandments to be followed are:

- moderation is the golden rule – do not eat much of any food.
- do not to reject any food, eat at least a little.
- eat one portion of all foods, The essence of a balanced diet is variety; the more the variety, the better is the nourishment; eating different kinds of food is desirable.
- all vegetable oils {except hydrogenated} are good in moderate quantity; use different oils by rotation.
- regularity of meals and having intervals of more than two hours between successive meals avoids disturbance in digestion.
- on special occasions one may eat more than usual and enjoy it without any guilt; it will be necessary to compensate later by eating light meals.
- avoid supplementation and fortified food.
- avoid indulgence with any one food/supplement that is deemed healthful: both omega-6 and omega-3 fatty acids are required by the body.
- do not blindly follow the advice of consultants or the media
- avoid soft drinks and processed foods.
- eat the least amounts of foods rich in sugar, fat and salt, e.g., dessert, fried food, cream, and pickles.
- instead of two square meals, eat five to six times a day without increasing total caloric intake.
- never waste money on commercially marketed micro-nutrients, fibre, anti-oxidants and flavonoids because all are present widely in condiments, spices, vegetables, fruits, germinated legumes, whole pulses, garlic, flaxseeds (*Javas*), fenugreek seeds (*Methi*) and tea without milk, etc.; and thus are adequately present in traditional diets.
- there is no need to force oneself to drink 8 or more glasses of water daily; adequacy of water is indicated by normal urine output and absence of thirst.

### **Conclusion**

In a nutshell, everyone should understand that the answer is clear. For good nutrition it is ideal to eat traditional diets and foods. Our 'normal foods' contain not only all the known nutrients, but also some unknown ones awaiting discovery and perhaps many others that will never be known. Traditional wisdom will also protect and save modern *homo sapiens* from 'mad man disease'!

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# **DRINKING WATER A UNIVERSAL MICRONUTRIENT CARRIER ANAEMIA PREVENTION WITH IRON FORTIFIED WATER**

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## **Introduction**

Micronutrient deficiencies are widespread, affecting a large proportion of the world's population. Deficiencies of iodine, iron, zinc and vitamin A are considered to be the most prevalent nutritional deficiencies. They are present mainly in the developing world and millions of persons are affected. Infants, preschool children and pregnant women are the major groups at risk of iron deficiency anemia. The problem is well known and has been studied for a long time. Its solutions include dietary improvement with a nutritious daily diet, the administration of pharmacological preparation supplements to vulnerable populations, and fortification of common foods with micronutrients. All these measures have been shown to work, under specific conditions:

- the food-based solution calls for changes in the dietary behaviour and possibly also the economic means of the population, and
- the periodic administration of solutions/tablets or capsules, although a relatively low-cost intervention, requires an effective delivery infrastructure and family compliance.

The fortification of commercial foods is considered to be responsible for the elimination of a variety of mineral and vitamin deficiencies in developed countries; fortification has also been used in developing countries, and certainly has advantages. Iron deficiency, which has been considered the most important nutritional problem in the world, is far from being solved and the feasibility of fortifying a suitable, readily available, and universal carrier has been considered. Several carriers have been used for delivering added iron, and some of these have been shown to be effective under local and/or experimental conditions, but their efficacy and long-term usability as universal carriers is yet to be demonstrated.

This situation in relation to iron fortification and iron carriers was recently highlighted at the recent Micronutrient Forum held in Turkey In 2007. Lectures and posters called attention to the importance of iron deficiency and iron deficiency anaemia, and recent studies on several aspects of the problem were presented. Nanoparticles of ferric phosphate were evaluated for solubility, bioavailability and safety. It was shown that these iron particle compounds have a bioavailability similar to the well established current standards. In Mexico, a food supplement fortified with iron gluconate for toddlers proved more effective in improving iron status and growth than a similar supplement containing ferrous sulphate. In Cambodia, iron-fortified fish sauce with 10 mg of iron from ferrous sulphate along with citric acid or NaFeEDTA proved effective in reducing iron deficiency and anaemia. In Vietnam, weekly supplements of multiple micronutrient-fortified biscuits reduced the prevalence of anaemia. There are also a large number of other

studies on the subject, investigating a variety of carriers fortified with iron, such as rice flour with iron formula premix in Mexico, soy sauce in Indonesia, and brown bread in South Africa. A micronutrient-fortified (including iron) beverage reduced anaemia in pregnant women in Cameroon by 56%. Mandatory wheat flour fortification with iron and folic acid, and of maize, is ongoing in Nepal and Pakistan. Wheat flour fortification was implemented in Brazil to deal with iron deficiency and it is of interest to report that the first results were said to be poor because the bread that was the iron carrier was not reaching the target population and would not be regularly available to them.

At the same time, fortification at the “point-of-use” or as “home fortification” with powdered vitamins and minerals has emerged as a new way to supply micronutrients. The powder would be added directly on the food. One of them, a product called “Sprinkles™” a multi-micronutrient powder packed in individual sachets, has been tried in several countries. The product is commercially produced, and specific strategies are in place for its marketing and distribution. It was tried in Afghanistan, Pakistan, Mali and India and the difficulty was that it was not being locally produced and would not fit in with local food habits. All these quoted examples and many other data from the literature show us that when a bioavailable source of iron is added to different carriers it will show good results, increasing iron blood parameters and decreasing iron deficiency anaemia. The major problem is that, in spite of successful local trials to deal with iron deficiency and anaemia, we are faltering in the overall battle. There has not been any decline in the prevalence of iron deficiency (ID) and iron deficiency anemia (IDA) all over the world; on the contrary, the numbers of persons with ID and IDA seems to be increasing world-wide.

There is no possibility, in the short term, that the problem of anaemia can be solved through the supply of a nutritious diet to the needy population. Production of medicinal iron supplements will require an adequate infrastructure, which is not available in most of the developing countries; what is more difficult is to put in place an effective health/nutrition delivery system. These facts will leave us with what was pointed out several decades ago by international organizations, namely, that food fortification is still the best approach to dealing with iron deficiency. Against the background of all that has been done so far, and knowing that the problem has to be looked at more as one of prevention than treatment, it is clear that the problem has to be solved through the use of a local suitable carrier, using locally available technology as much as possible. Considering also that fortificant compounds certainly will need to be imported, the studies of our group in relation to the problem of iron anaemia is that the best approach is to use drinking water as the most appropriate iron carrier. Therefore we would like to report the results of our studies on the utilization of drinking water as a universal natural iron carrier.

Water is available and used daily everywhere by everyone. Water can be utilized as a potential carrier for any soluble micronutrient; and it is known that the bioavailability of iron increases with its solubility. We have also used

drinking water as an iodine carrier, and it worked in pilot studies. We prepared, locally, a concentrated water-iron solution in bottles and added it to the drinking water in homes and day-care institutions. Lately we are also making sparkling or bubbling pills with iron salts and/or other soluble compounds such as ascorbic acid. These pills can be added to cooking or drinking water, making iron and other nutrients available to all the members of the family. We also suggest that micronutrients could be made commercially available as tablets, making it easier for the common people to use them in cooking, or through dissolving them to a suitable dilution in a water container of known volume at community level. This iron fortification of water does not require intensive cooperation or individual compliance. It will be a local community programme. It is a low cost, practical and effective approach and certainly could deliver small amounts of iron daily to all segments of the population including mothers, infants and small children at homes or public institutions. A summary of our work on the subject is given here.

### **Drinking water as an iron carrier to control iron deficiency and anaemia: experimental and community studies**

Fortifying drinking water locally with iron compounds was shown to be a feasible strategy from the physical and experimental point of view, operationally viable in various community settings, biologically effective, accepted by children, low in costs, and manageable with the available local infrastructure in several parts of Brazil. It is a practical way to supply iron (as well as other micronutrients) directly to the population to prevent and control iron deficiency, and it can reach rural as well as urban low socio-economic communities worldwide. Drinking water also has advantages over alien or unfamiliar fortified carriers or industrialized products brought from other countries. Water is available everywhere and is drunk everyday by every person. People have to learn how to keep water safe for drinking and certainly it can be easily fortified.

Drinking water as a micronutrient carrier is seldom quoted in the literature. In the 1998 USAID publication on food fortification in developing countries, water is cited as a possible carrier, but no details on its use are included. A few years ago, the World Health Organization organized a meeting and printed a 2005 publication on nutrients in drinking water. Several aspects of water were reviewed, including requirements, essential nutrients in drinking water, water minerals and cardiovascular diseases, etc but there was practically no reference to the use of drinking water as a micronutrient carrier, except in the context of fluoride. Fluoride has been added to drinking water for years and has been shown to be efficacious and effective in preventing dental carries. There has been some utilization of micronutrient fortification in beverages, including fortification with iron compounds. Iron-and-micronutrient-fortified beverages have been shown to reduce anaemia and improve haemoglobin concentration. Our group has been using drinking water as an iron carrier for years. It is shown to be an alternative means of supplying iron to preschool children at the community level.

### ***Studies on the utilization of drinking water as a vehicle for nutrients: laboratory and experimental studies in rats***

The objective of these laboratory experiments was to show the effect of adding various inorganic iron salts to drinking water and checking their effects on colour, turbidity and taste, through physical and chemical tests, along with acceptability trials carried out in children. Ferric ammonium citrate, Fe chloride, Fe gluconate, Fe hydroxide, Fe sulphate, and Fe nitrate, diluted in water, were tested. Iron citrate, chloride, gluconate and ferrous sulphate produced small colour changes at 1mg/L and 5 mg/L concentrations, when measured initially and after seven days. Tests with iron sodium EDTA added to the water solution showed practically no colour change and no metallic taste, and the solution remained clear and transparent. The presence of chloride in iron-fortified water increased the water colour and turbidity in the ferrous sulphate solution, though it had no effect on the NaFeDTA solution. Along with the physicochemical tests, acceptability trials of these various water-fortified solutions were carried out in more than 500 children. It was also shown that water turbidity decreases with the addition of ascorbic acid or citric acid to the solution. Water solutions of Fe gluconate, citrate and sulphate had less colour and turbidity than  $[\text{OHFe}^3 \text{ polymaltosed}]$  and  $\text{Fe}^3 \text{ nitrate}$ . Experimental studies in rats showed that, after a 35-day supplementation with ferric ammonium citrate, ferrous sulphate and ferrous gluconate their Hb levels rose from 8-9 to 13 g/dL. The controls receiving no iron and the animals drinking iron fumarate had unaltered mean Hb levels of approximately 8 g/dL.

### ***Drinking water as an iron carrier to control anaemia in preschool children in a day-care centre***

This study examined the impact of iron-fortified drinking water offered to 31 preschool children attending a day-care institution in the city of Ribeirão Preto over a period of eight months. Children from low socio-economic families stay 5 days a week at a day-care centre, from 7 am to 5 pm. Iron sulphate solution was added to their drinking water, at a concentration of 20 mg of elemental iron per litre. Clinical and anthropometric data were obtained for each child. Blood was collected and haemoglobin and serum ferritin were measured before intervention and at four and eight months after intervention. The prevalence of anaemia decreased after the introduction of iron-fortified drinking water (ferrous sulphate only). After eight months of ingestion of iron fortified water, mean haemoglobin values increased from 10.1 to 13.7 g/dL and serum ferritin rose from 13 to 25.6 mcg /L.

### ***Iron fortification of domestic drinking water to prevent anaemia among low socio-economic families in Brazil***

The objective of this study was to evaluate the effects, at the household level, of an iron-fortified drinking water programme in the city of Ribeirão Preto. We investigated the changes in haemoglobin and ferritin levels of parents and their small children who attended the University Hospital and had blood haemoglobin levels suggesting borderline anaemia. Twenty-one young, low-socio-economic section families comprising 88 subjects participated in the

project and were divided into two groups. For a duration of four months, twelve families (22 fathers and mothers and 22 children under the age of 6 years) with haemoglobin levels  $\leq 11$  g/dL were given a solution of iron + ascorbic acid (AA) in water in small flasks to add to their drinking water and cooking water container (final concentration 10 mg of Fe and 60 mg AA/L), while 9 other families (18 fathers and mothers and 26 small children) were supplied with the same type of water, but without any added iron or ascorbic acid. Blood samples were collected at the beginning and at the end of the trial to determine Hb and ferritin levels in both children and adults. The group receiving the iron and ascorbic acid fortified water showed an improvement in Hb and ferritin values while the control had unaltered Hb and ferritin concentrations.

***Effect of fortification of drinking water with iron plus ascorbic acid or with ascorbic acid alone on haemoglobin values and anthropometric indicators in preschool children in day-care centres in Monte Alto, Southeast Brazil***

The importance of ascorbic acid (AA) in promoting iron absorption has been established. The objective of this trial was to focus on the effect of ascorbic acid on iron utilization. The study was carried out in 150 children attending 6 day-care centres in the village of Monte Alto. Their diet contained approximately 10 mg of iron, mainly from vegetable sources, and low levels of vitamin C (28% of daily requirements for the age group). During the six-month period of the study, half of the children received iron plus 100 mg of AA in the water and the other half received only the 100 mg AA, with no added iron. The prevalence of anaemia (Hb  $\leq 11$  mg/dL) was 45% in the iron plus AA group and 31% in the AA group, at the beginning of the experiment, dropping to 31.7% and 17.1%, respectively, at the end of the study. We had previously shown that fortification of orange juice with iron (8 mg a day) offered to preschool children for a period of four months increased their haemoglobin levels significantly.

***Effects of the intake of iron-fortified drinking water on blood values of preschool children, Ribeirão Preto, Southeastern Brazil***

Biochemical and haematological examination, including a complete blood count with estimations of haemoglobin, haematocrit, MCV, MCH, MCHC, serum iron, percentage of saturation of haemoglobin, total iron-binding capacity, serum ferritin, serum transferrin receptor, and red blood cell morphology, were carried out in 488 preschool children of ages 0.5 to 4 years in 12 day-care centres in the city of Ribeirão Preto. They were given water fortified with ferrous sulphate plus ascorbic acid (Fe 15 mg/L + AA 90 mg/L) or with iron sodium EDTA (15 mg/L) and their blood samples were collected at 0, 6, and 12 months afterwards. The prevalence of anaemia decreased. Overall, the iron status of the children improved. The improvement was similar in children receiving iron sulphate and in those receiving NaFeEDTA. In a sub-sample of 65 children who received ferrous sulphate and who had similar blood values at six and twelve months, haemoglobin levels increased ( $p < 0.01$ ) and mean corpuscular volume, corpuscular haemoglobin, corpuscular

haemoglobin concentration, and MCV increased significantly ( $p < 0.0001$ ) after intervention. Abnormal red cell morphology was seen at the beginning of the study, but this decreased during the year. There was no clear pattern related to the fortification intervention.

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# MALNUTRITION IN EARLY LIFE CONSEQUENCES FOR ADULT HEALTH AND HUMAN CAPITAL

Fall C

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## Introduction

Nearly twenty years ago, it was reported that low birth weight and low weight in infancy were associated with an increased risk of adult hypertension, Type 2 diabetes and cardiovascular disease (CVD). This led to a controversial hypothesis that, along with genetic factors and adult lifestyle, exposure to undernutrition in very early life increases an individual's vulnerability to these disorders, by 'programming' permanent structural and metabolic changes. Animal experiments have provided proof-of-principle that maternal undernutrition can produce these outcomes in the offspring, and that the effects can be prevented by nutritional interventions. For example, in rats, maternal protein restriction during pregnancy leads to elevated blood pressure in the offspring, and this is prevented by supplementing the mother's low-protein diet with folic acid. Animal studies have revealed mechanisms that could mediate disease in later life, including effects of early undernutrition on endocrine pathways and epigenetic characteristics. Implicit in the programming hypothesis is the assumption that, since the mother's nutritional status influences the quality and quantity of nutrients reaching the foetus, improving the nutrition of girls and women can prevent common chronic diseases in future generations. If true, this could be particularly important for India, where maternal undernutrition is widespread and where diabetes and cardiovascular disease are becoming major problems.

## Contributions of Indian scientists

Research scientists from India have made major contributions in this area, showing that children with lower birth weight have higher insulin resistance and metabolic risk factors for CVD, and that adults who were born with lower birth weight have a higher risk of coronary heart disease. Data from a unique longitudinal birth cohort in Delhi has shown that the risk of adult disease is modified by post-natal as well as pre-natal factors; low infant weight and rapid gain in weight during mid-childhood and adolescence increase the risk of developing type 2 diabetes in later life. Indian investigators have contributed to the progress in understanding the role of specific nutrients in the maternal diet and their possible impact on disease risks in the offspring. In the Pune Maternal Nutrition Study, low maternal vitamin B12 status (prevalent in 70% of rural mothers) predicted increased childhood adiposity and insulin resistance in the offspring, especially if the mother was folate-replete. Studies in India have shown that it is not only maternal *under*nutrition that causes problems; gestational diabetes, which causes a form of foetal *over*nutrition (glucose excess), is also associated with increased adiposity and insulin resistance in the children. This highlights the adverse effects of the so-called 'double burden' of malnutrition in developing countries, where undernutrition and overnutrition co-exist in the same community or even in the same individual.

## **Impact of improvement in maternal nutrition**

What would be the impact on the offspring, following interventions to improve maternal nutrition? This was an area in which studies have been much awaited. In the past year, several longitudinal follow-up studies relating to such offspring have been reported from around the world. They show that some CVD risk factors can be improved, but results differ depending upon the population, the specific intervention, and the post-natal environment. Ongoing studies in India and elsewhere will increase our understanding of the long-term effects of nutritional status in early life, and how best to translate this knowledge into policies to improve the health of future generations.



# **MILLENNIUM DEVELOPMENT GOALS RELATING TO POVERTY, HUNGER AND MATERNAL AND CHILD MORTALITY: THE PHILIPPINES EXPERIENCE**

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*Dr. C. Gopalan is a world-renowned nutrition scientist. He towers over other scientists in his ability to use his brilliant scientific mind, while remaining deeply sensitive to the daily struggles and aspirations of his people and keenly aware of global developments and challenges. A lasting tribute we can offer to the guru of nutrition in Asia is to maintain our pride of place in this field by (to use his own words) “seeking, fostering and cherishing practices of ours in Asia that are conducive to general health and well-being.” Truly the Asian house of nutrition has deep historical foundations and a treasure trove of sound practices born out of learning by living.*

## **Introduction**

The Philippines is a signatory to the United Nations Millennium Declaration that was adopted by heads of State and Government at the General Assembly of the United Nations in September 2000. It agreed to a set of time-bound goals and targets towards reducing extreme poverty and various forms of human deprivation. This paper describes and reviews the country's experience as presented in the Philippines Progress Reports on the Millennium Development Goals (MDG), the preparation of which was coordinated by the National Economic and Development Authority with financial assistance from the United Nations Development Programme. It focuses on three goals: eradication of extreme poverty and hunger, reduction in child mortality, and improvement in maternal health, based on the MDG reports in 2003, 2005 and 2007<sup>1-3</sup>.

## **The Philippines government's 2007 MDG report**

Table 1 shows the country's rate of progress towards achieving these three goals and the probability of attaining the targets. Using the ratio of required rate of progress necessary to reach the target to the average annual rate of progress, the probability of reaching the target by 2015 was arbitrarily categorized as “high” for ratios less than 1.5, “medium” for ratios of 1.5-2.0, and “low” for ratios greater than 2.0. On this basis, the government concluded that there is a high probability of attaining the target for reduction of extreme poverty, hunger and child mortality, but only a low probability with regard to the goal for reduction of maternal mortality. One of the MDG targets was to reduce by fifty percent the proportion of people living in extreme poverty. A surrogate indicator used was the proportion of the population below the subsistence or food threshold, defined by the government as the income needed by a person to pay the cost of a recommended minimum food basket. As of 2003, the proportion of people in extreme poverty was 13.5% (more than 10 million) as compared to the baseline figure of 24.3 percent in 1991, giving an average decline of 0.9% per year (compared to the required

<b>Table 1: Philippines MDG's rate of progress at the national level</b>							
MDG Goals and Targets	Baseline (1990 or year closest to 1990)	Current Level (2005/2006 or year closest to 2005/2006)	Target by 2015	Average Rate of Progress (1990 – 2005/06 or year closest to 2005/06) (a)	Required Rate of Progress (2005 / 2006 – 2015) (b)	Ratio of Required Rate to Average Rate (I =b/a)	Probability of Attaining the Targets
<b>I Eradicate extreme poverty and hunger</b>							
Proportion of population below subsistence threshold	24.3	13.5 (2003)	12.15	-0.9	-0.11	0.13	High
Prevalence of malnutrition among 0-5 year-old children based on international standards	34.5	24.6 (2005)	17.25	-0.66	-0.74	1.11	High
Proportion of households with per capita intake below 100% dietary energy requirement	69.4	56.9 (2003)	34.7	-1.25	-1.85	1.48	High
<b>II.Improve maternal health</b>							
Maternal mortality rate	209	162 (2006)	52.2	-3.62	-12.2	3.37	Low
<b>III.Reduce child mortality</b>							
Under-five mortality rate (per 1000 live births)	80.0	32.0 (2006)	26.7	-3.0	-0.59	0.2	High
Source: Philippines Midterm Progress Report on the Millennium Development Goals 2007							

reduction rate of 0.11 for the remaining years up to 2015). With a ratio of 0.13, the country has a high probability of meeting the 2015 target of having just 12.15% of the population still living in extreme poverty. The data sets used for tracking poverty come from the Family Income and Expenditure Survey undertaken periodically by the National Statistics Office.

Two indicators are used to monitor the country's progress in addressing hunger. These are:

- the proportion of households with per capita food intake that provides less than 100% of the Philippines recommended dietary energy requirement, and

- the proportion of under-five-year-old children who are underweight for their age based on an international reference standard (NCHS/WHO). In terms of each of these indicators there is a high probability that the 2015 target will be met. The average annual rate of decline in prevalence of underweight was 0.66% from 1990 to 2005; also, the population with inadequate energy intake declined at an average rate of 1.25% from 1993 to 2003. The data sets to monitor underweight and energy intake come from the National Nutrition Survey (NNS) conducted periodically by the Food and Nutrition Research Institute of the Department of Science and Technology.

For the goal relating to reduction of child mortality, the target is to reduce the mortality rate of under-five children (U5MR) by two-thirds before the year 2015. The reference data came from two different sources: baseline data for 1990 from the government's Technical Working Group on Maternal and Child Mortality and 2006 data from the Family Planning Survey of the National Statistics Office. With an average annual reduction rate of 3.0% as compared to a required reduction rate of 0.59%, there is a high probability that the 2015 target of reducing child mortality to 26.7 deaths per 1000 live births will be attained by 2015.

Unlike the targets for poverty, hunger, and child mortality, the target to reduce maternal mortality rate (MMR) by three quarters before the year 2015 is not only unlikely to be met but “the least likely to be achieved for the Philippines,” according to the 2007 MDG Report. The required annual rate of reduction is more than three times the average rate of reduction from 1993 to 2006. The 1993 and 1998 National Demographic and Health Surveys and the 2006 Family Planning Survey indicated a decline in MMR but at a sharply diminishing rate, from 209 deaths per 100,000 live births in 1993 to 172 deaths in 1998 and 162 deaths in 2006. The government has attributed the slow decline in MMR to inadequate prenatal care, high incidence of high-risk births, and inadequate information and means to manage difficult pregnancies.

### **Promotion of maternal health**

The three major causes of maternal deaths in the country are postpartum hemorrhage, eclampsia and severe infection<sup>3</sup>. Citing the 2006 study of the Allan Guttmacher Institute, the 2007 MDG Report indicated that, out of three million pregnancies that occur every year, half are unplanned and one-third of these end in abortions. Young women accounted for 17 percent of induced abortions, the fourth in the list of leading causes of maternal death. The Department of Health recommends that all pregnant women must have at least four antenatal care visits during each pregnancy, and the first antenatal checkup should occur in the first trimester of pregnancy. Based on the 2003 National Demographic and Health Survey or NDHS<sup>4</sup>, 70% of women who had given birth to a live infant in the five years preceding the survey met the criterion relating to the recommended number of visits, but only 53 percent had received a checkup within the first three months of pregnancy. Half of all the women who received antenatal care were informed of pregnancy

complications such as vaginal bleeding, paleness or anemia. About 77 percent said they received iron tablets or syrup during their most recent pregnancy (there was no information on frequency or duration of supplementation).

For many years, the government had been undertaking a programme of iron supplementation. The National Guideline on Iron Supplementation stipulates that one tablet containing 60 mg elemental iron and 400 mcg folic acid be given daily for 180 days to pregnant women, and for 90 days to lactating women; there are also specified doses and durations for infants, children of ages 1-5, and for anaemic and underweight 6-12 year-old children. In the 2003 NNS<sup>5</sup>, 44% of pregnant women were found to be anaemic, the same rate of prevalence as was found a decade earlier.

In 2008, the programme was assessed by the National Nutrition Council (NNC) as a “token” one, since the outreach is “so minute” compared to the total needy population<sup>6</sup>. For a “more realistic focus of interventions on infants and pregnant women” the NNC made two important revisions in its target for 2010. It de-listed 1-5 and 6-12 year-old children as targets for iron supplementation (the prevalence of anaemia in these groups of children was ~30-40%). It also revised the target for anaemia reduction in infants by as much as 18%; the original target of 41.7% was raised to 59.3%. In 2003, 66% of infants of ages 6 months to less than one year were anaemic, a figure 35% higher than in 1993. The original target for anaemia reduction in pregnant women, from 43.9% in 2005 to 42.1% in 2010 (a measly 0.36% average annual reduction), was retained. Here is an instance where a commitment to the MDG did not manifest itself in more aggressive efforts to undertake what is necessary to address a problem.

The target relating to MMR reduction is linked to the target relating to reproductive health services. In fact, the very slow decline in MMR may be traced to inadequate access to integrated reproductive health services. According to the 2007 MDG Report, there is a low probability of doubling the prevalence rate of men and women/couples practicing responsible parenthood, from 40 in 1993 to 80 in 2015. There are several reasons for this rapid population growth, poor access to contraceptive care, gender norms in the family and community, and cultural and religious beliefs and practices.

One of the biggest challenges in the country is to decisively adopt a clear and consistent population policy. There is an urgent need for the national government, through the legislature, to pass a law that unequivocally states its policy with respect to population growth management, reproductive health and the objectives of the national family planning programme. In this connection, greater attention should be given to adolescents. Based on the 2000 Census, Filipinos 15-24 years of age accounted for 15.1 million or 19% of the total population of the country<sup>3</sup>. There has been an increase in the percentage of those in this age bracket who have had premarital sex, and in the number of teenagers who have begun childbearing, with the latter being much higher among rural and less-educated girls.

The Medium-term Philippine Plan of Action for Nutrition 2005-2010 (MTPPAN) declares “strategic focus on adolescent females, pregnant and lactating women and children 0-3 years old”<sup>7</sup>. However, it does not include adolescent females among those for whom key performance indicators were spelled out in relation to the nutritional problems that are to be addressed during the five-year period. The earlier reference to adolescent females, whose inclusion was justified in terms of a life-cycle approach to malnutrition and risks to the well being of both mother and child, was deleted when the MTPPAN was updated for 2008-2010.

The United Nations Population Fund<sup>8</sup> put it beautifully when it stated that adolescence can be neither denied nor seen as “a time between,” because the goals that adolescents set for themselves are not just preparatory, but are meaningful parts of their lives. It argues that the choices that young people make can set them on courses that can benefit or harm them, their families, friends and communities, and this makes it necessary to provide them adequate information, opportunities, resources and support to guide their choices.

Dr. Gopalan pointed out that there are currently no imaginative programmes for sensitizing the young people, especially the adolescents, to the health problems we face<sup>9</sup>. In order to mobilize the youth, he recommends a National Health Scout Movement wherein both boys and girls would enroll in suitable training programmes to sensitize them to major health and nutrition problems, and to train them to be “agents for change” to promote health and nutritional well-being in their families and in the community. To the list of instruction modules that he recommends, which includes first aid, healthy lifestyles and dietary practices, environmental hygiene and good citizenship; I would add reproductive health and responsible family planning.

The government has introduced several key policy reforms to reduce maternal mortality, and has undertaken an aggressive two-pronged strategy involving the provision of health services to pregnant woman and provision of family planning services<sup>3</sup>. An important policy reform is the adoption of the “emergency obstetric care approach” which considers all pregnant women to be at risk of complications at childbirth. This replaces the “risk approach” which identifies high-risk pregnancies for referral during the prenatal period. A much more supportive environment to promote maternal health is needed at various levels:

- improved access to health care;
- effective programme implementation;
- availability and sustainability of financial and other resources;
- accelerated institutional and human capacity building, particularly in view of the devolution of health-care services to local government units; and
- rationalization of the country's health personnel programme considering the large rural-to-urban movement and the migration of health workers abroad.

## Vitamin A supplementation

The first MDG Report identified universal vitamin A supplementation of young children as one of the four factors responsible for reduction in U5MR. It is not clear how the government arrived at this conclusion. But what the NNS data show is increasing prevalence of vitamin A deficiency (VAD), based on serum retinol evaluation, among children under five, from 35% in 1993, to 38% in 1998, to 40% in 2003. In fact, in 1998 VAD was a public health problem in all regions of the country, with prevalence rates ranging from 26% to 55% in children between the ages of 6 months and five years.

Universal vitamin A supplementation of children from 6 months to 71 months of age was launched in the country in the 1990s despite the fact that, based on both biochemical and clinical findings, VAD was not a significant public health problem, except in one region of the country<sup>10</sup>. It became the focus of the country's nutrition programme,<sup>11,12</sup> and it had what may be called the elements for success, such as a policy in place; adequate national and international support; active participation of the private sector, media and non-government organizations, strong involvement of local governments, and intensive capacity building. After more than a decade of universal supplementation, there has not been any decline in VAD in the country. This has baffled the government. Thinking that the problem may be the result of poor coverage, a house-to-house campaign by village health and nutrition workers was adopted. However, as the NNC itself declared, higher coverage and food fortification did not translate into lower levels of VAD<sup>6</sup>. A recommendation to adopt a policy of thrice-a-year administration<sup>13</sup> was initially considered by the NNC. However, it was not pursued because of limited resources for implementation. But even if the government has the resources, the recommendation should be considered only after adequately studying its feasibility, safety, efficacy and effectiveness. Indeed, at this point, the priority should be not only to undertake proper studies to determine what ails the country's vitamin A supplementation programme, but to seriously explore other approaches, primarily food-based programmes, and to improve the understanding of underlying factors.

The NNC's claim of the positive influence of supplementation on micronutrient deficiencies and underweight in young children led to the inter-departmental agency's policy of adopting, starting in 1993, a strategy involving a heavy investment in vitamin A supplementation. This thrust continued up to the formulation of the 2005-2010 MTPPAN, which initially targeted a 63% VAD reduction in young children, from 40.1% to 14.9%. However, in the Updated MTPPAN 2008-2010, the NNC changed the target to "more reasonable" levels by setting an arbitrary 10 percent decline in prevalence<sup>6</sup>. Thus, in the second instance, a commitment to the MDG did not spur the government to more aggressively address a problem, the resolution of which is considered important for the attainment of one of its goals. Recourse was taken, once more, to resetting the target downward.

The priority action plan drawn up by the government to eradicate extreme poverty and hunger is rather intriguing. This refers to priority action number

10, which relates to arresting the increasing trend towards overweight and obesity<sup>2</sup>. By what means, direct or indirect, short-term or long-term, could such an action reduce the proportion of households below the minimum level of dietary energy consumption and proportion of underweight young children? An explanation of perceived links between the planned action and the specific target would be instructive.

### **Beyond national sums and averages**

There are several ways of tracking a country's progress in human development. National averages and changes at various periods are informative, but not nearly enough for a deeper and better understanding of not only the state of affairs but also its contexts and implications. For example, although the Philippines appears to have a high probability of meeting its goal relating to poverty reduction, a noted economist<sup>14</sup> pointed out that the country should be doing better than simply cutting the prevalence of extreme poverty by half. The prevalence of poverty is, to begin with, alarmingly high compared to some of the neighbouring countries (citing World Bank data on the proportion of the population subsisting below US\$ 1 a day, the prevalence is 11% in the Philippines, 7% in Indonesia and 2% in Vietnam). Yet another example is the reported on-track progress towards reduction of child undernutrition. Data from the country's three last NNS<sup>15</sup> indicate a slowing down of the rate of progress in reducing child undernutrition, with the average annual rate of reduction of underweight in children under five years of age being 1.85% from 2001-2003 and 1.15% from 2003-2005. Based on the projected population, 3.7 million Filipino children were underweight for age in 2005. Moreover, according to the UNICEF's 2006 Report Card on Nutrition<sup>16</sup> just ten countries account for the 146 million underweight children under five years of age in the developing world; these are, in descending order of magnitude, India, Bangladesh, Pakistan, China, Nigeria, Ethiopia, Indonesia, Democratic Republic of the Congo, the Philippines and Vietnam. The same source reported the country's average annual rate of reduction of underweight in this age group to be 0.9% for the period of 1990-2004, which is much less than the rate observed in six of the ten Asian countries in the list.

A notable feature of the third and latest MDG Progress Report is the inclusion of information at the sub-national or regional level. Table 2 presents the rates of progress towards the selected targets of the MDG in every region of the country. All the regions have a high probability of reaching their target for U5MR, 82% of them have a high probability of reaching the goal relating to reduction of the proportion of households below the subsistence threshold, and 59% of them have a high probability of achieving the goal relating to reducing the prevalence of underweight in children. On the other hand, only 35% of the regions have a high probability of reaching their target for household energy intake and 47% for achieving the MMR goals. The Philippine government estimated as 56.9% the proportion of households with inadequate energy intake. An analysis of the data from the 16 regions for which such data was available show that half of them have higher percentages than the national figure. Moreover, these same regions have

slower average annual rates of reduction, ~0.6% compared to 1% to 2% for regions with less than the national average. Since all regions report ~50 – 60% of households with inadequate food energy intake, at least one in every 3-4 households will be without adequate food even if the 2015 target were to be met. It also bears noting that while the average intake of Filipinos is 98 percent of energy requirement, three nutritionally vulnerable groups have much less intake than this: 83% for infants and children under five, 78% for pregnant women and 75% for lactating women.

### The road ahead

The Medium-term Philippine Development Plan 2004-2010<sup>17</sup> states that the country's development efforts are directed towards achieving the MDG in 2015. As the country marks the halfway point in its commitment to achieving the MDG, it appears to be on track in terms of the goals that are most closely related to nutrition, in particular, reduction of extreme poverty, hunger and child mortality. But even so, the Philippines face a huge challenge in addressing wide disparities in human development across the various regions

Region	Proportion of population below subsistence threshold	Prevalence of malnutrition among 0-5 year-old children	Proportion of households with per capita intake below 100% dietary energy requirement	Under-5 mortality rate (per 1,000 live births)	Maternal mortality rate
CAR	High	High	Low	High	High
I	High	Medium	High	High	High
II	High	High	High	High	High
III	High	High	Medium	High	High
IV-A	High	High	Low	High	High
IV-B	Low	Low	High	High	Low
V	High	High	Low	High	Low
VI	High	High	High	High	Low
VII	High	High	Low	High	High
VIII	High	Low	Low	High	Low
IX	Low	Low	Low	High	Low
X	High	Medium	Medium	High	Low
XI	High	High	High	High	High
XII	High	Medium	Medium	High	Medium
CARAG A	Low	High	No baseline	High	Low
ARMM	High	Low	Low	High	High
NCR	High	High	High	High	Medium

Source: Philippines Midterm Progress Report on the Millennium Development Goals 2007



of the country. Not very long after the issuance of the latest MDG Progress Report in 2007, the government released the results of the 2006 Family and Income Expenditure Survey<sup>18</sup>. The good news is a decline (albeit very slightly) in the Gini coefficient from 0.4605 in 2003 to 0.4565 in 2006. The bad news is an increase in the number of Filipinos living below the subsistence or food threshold from 10.8 million in 2003 (14.6% of the population or 11% of all families) to 12.2 million in 2006. Additionally, the poorest 30% of households spent much more on food, which meant having less to spend on other basic needs.

The unrelenting increase in the price of oil and oil products affected the whole world. With the consequent increase in the cost of goods and services, the inflation rate in the Philippines rose to the highest level in 14 years. The price of rice alone, the staple food of Filipinos, went up by 43%. Prices are rising rapidly and large numbers of jobs are being lost. In the face of these difficulties, the government aggressively launched a series of what it calls pro-poor programmes, using, ironically, its increased revenue collection from the implementation of the expanded value-added tax on oil and oil products. Some examples are low-cost rice for the poor, one-time cash aid to help the poor pay their electricity bills, fertilizer subsidy to poor farmers, and fuel subsidy to the public land transport sector and cash aid to help families with the schooling of their children. The doles given by the government no doubt help to alleviate the sufferings of the poor to some extent. But clearly this form of assistance cannot be sustained. The government realizes that, in order to strengthen people's self-reliance it must more resolutely pursue policies and programmes to improve employment opportunities, mobilize domestic resources, accelerate basic health and education reforms, curb population growth, and hasten equitable sharing of income and wealth.

What lies ahead for the Philippines in terms of the MDG in the remaining years toward the 2015 finish line? The crisis that affects the country fogs the view of the future, but it should not have the same effect on the core values of the United Nations Millennium Declaration of 2000. The Declaration is not only about goals and targets. It is, first of all, at least on the basis of the presentation in the document, about fundamental principles such as equity and social justice. It is also about good governance, protecting the vulnerable, and ensuring a shared responsibility on the part of national and international communities in working towards achieving these goals.

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# CHANGING PROSPECTIVES AND PRIORITIES IN ICMR FOR NUTRITION RESEARCH

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## Introduction

The Indian Council of Medical Research (ICMR), the apex body in India for the formulation, coordination and promotion of biomedical research, is one of the oldest medical research bodies in the world, which will be completing its 100 years in 2011.

The “Green Revolution” has boosted production of wheat and rice, the staple cereals of people in the country and accounting for 70-75% dietary energy and most other nutrients. The spectacular increase in production has been offset by the rapid population growth. Nevertheless, the nutritional status of poor children has not deteriorated, but has shown some improvement. Disease like cardiac beriberi, peripheral neuritis, burning feet syndrome and pellagra which used to be major public health problems in the 1950s, and early 1960s, have disappeared. Kwashiorkor of the classic kind (fat, blubbery child with crazy-pavement skin) has steeply declined. Keratomalacia, which used to be a major cause of nutritional blindness in children till the 1960s has now almost disappeared. Goiter/IDD, which was major public health problem in 1960s, has been reduced considerably. Similarly, prevalence of another micronutrient deficiency (Vitamin A) has also come down considerably. To combat anaemia technology of double fortification of salt with Iodine and Iron was developed. In last one decade emphasis was given on Genetically Modified foods and stem cell research and accordingly capacity building was developed considerably.

## Beginning of nutrition research in India

Nutrition research in India was started in 1918 when Sir Robert Mc Carrison set up Beri–Beri Enquiry Unit in a single room laboratory at the Pasteur Institute, Coonoor, Tamil Nadu. The unit blossomed into a “Deficiency Disease Enquiry” within seven years and later in 1928 emerged as full-fledged ‘Nutrition Research Laboratory’ with Dr. Mc Carrison as its first Director. The laboratory was shifted to Hyderabad in 1958 and was renamed as -National Institute of Nutrition (NIN) in 1969.

What I liked best in Dr. Gopalan is clarity in thinking and his passion for nutrition research. His connectivity with subject was remarkable. When I became Director General, ICMR in 1998, I met him in India International Center and we had intense discussion about nutrition research in ICMR. While I sought his view, expressed my ideas too. He had a patriotic attitude in his thinking. Whenever we had difference of opinion, we set together, discussed and sorted it out.

*N K Ganguly*

<sup>1</sup> Former DG, ICMR, Currently Distinguished Scientist, Department of Biotechnology, New Delhi, India

<sup>2</sup> Indian Council of Medical Research, New Delhi, India

## **Nutrition research at NIN and at ICMR**

Nutrition research in ICMR was mainly carried out by NIN till 1980. In late seventies and early eighties ICMR initiated the Task Force strategy for centrally coordinated studies in various areas including “nutrition” as extramural research. The task force approach emphasized a time bound, goal oriented approach with clearly defined goals, specific time frames, standardized methodologies and often a multicentre structure. Besides, ICMR has also been playing supportive role by providing financial assistance to individuals from various institutes/ Organizations of the country for carrying out nutrition research. An advance centre for policy and programme analysis has also been set up as extramural research programme.

The setting up of the Food and Drug Toxicology Research Centre (FDTRC) in 1971, National Nutrition Monitoring Bureau (NNMB) in 1972 and National Centre for Laboratory Animal Sciences (NCLAS) in 1976 in NIN, Hyderabad and initiation of several multicentre Task Force Studies in ICMR Headquarters boosted Nutritional Research in ICMR.

The FDTRC later on in 1978 was established as separate centre in NIN Campus. The mandate was to investigate food borne disease outbreaks and undertake toxicological evaluation of foods and drugs. The Centre is also engaged in environmental monitoring as well as biomonitoring to study human exposures to carcinogens/toxins in the environment and their biological impact.

I had an opportunity to discuss various issues related to medical research and role of ICMR with distinguished scientists likes Dr. V.Ramalingaswami, Dr. P.N.Tandon, Dr. B.N. Tandon and others. On one of the occasions Dr. Gopalan was also present. We used this opportunity and also discussed about his baby NFI. I could now see that the deliberation then was very rewarding and NFI is gaining strength and moving towards sustainable foundation with strong effects in North India.

*N.K.Ganguly*

## **National Nutrition Monitoring Bureau**

National Nutrition Monitoring Bureau (NNMB) was established in the year 1972, with a Central Reference Laboratory at NIN and units in the states of Andhra Pradesh, Gujarat, Karnataka, Kerala, Madhya Pradesh, Maharashtra, Orissa, Tamil Nadu, Uttar Pradesh and West Bengal. Since then the bureau has been collecting data on dietary intakes and nutritional status of the population on a continuous basis. The bureau has also been evaluating the on-going National Nutrition Programmes, identifying their strengths and weaknesses and recommending mid- course corrections to improve their effectiveness.

## **National centre for laboratory animal sciences**

The National Centre for Laboratory Animal Sciences was set up with the aim of producing quality laboratory animals for experimental purposes. The centre

was known as the Laboratory Animals Information Service (LAIS) prior to 1976 and had its modest beginning in 1957 in Bombay. In 1959, the Centre was taken over by ICMR and later in 1976; it was shifted to the premises of National Institute of Nutrition (NIN), Hyderabad and renamed as Laboratory Animal Information Service Centre (LAISC). The activities of the centre were expanded and started breeding and supplying laboratory animals to various Institutions in the country. In 1988 with the financial support from ICMR and Department of Biotechnology, the services of LAISC were considerably improved through the establishment of a National Infrastructure Facility for Laboratory Animals (NIFLA). In the year 1995, the two centres, viz., LAISC and NIFLA were merged into a single unit and re-christened as the National Centre for Laboratory Animal Sciences (NCLAS). The center is currently meeting the breeding and experimentation needs of over 180 institutions in the country. Currently the centre is focusing on, to breed and supply genetically and microbiologically defined laboratory animals; to import and supply selected strains of laboratory animals for biomedical research; development of natural mutants for study of human diseases; conducting research in laboratory animal sciences; human resource development by organizing regular training courses; to disseminate information through Information-Education- Communication; to serve as a national reference centre and nodal agency on matters related to laboratory animal science and technology.

I met Dr. Gopalan in 1949 when he returned from England after completing his Doctorate. He is a smart organizer, dynamic and very disciplined commander. He has unique ability to guide scientific work in different disciplines. After Dr. Gopalan took over as Director NIN, there was tremendous expansion of the institute. This includes construction of Staff Quarters, expansion of Library etc. During his tenure very important activities were launched such as NNMB.

*P.G.Tulpule*

### **ICMR extramural research in nutrition**

Under extra mural research several multicentre studies have been carried out by ICMR headquarters in last 25 years in different areas of Food Safety & Nutrition. These studies have generated useful data/ information for policy makers and programme managers.

Nutritional anaemia is a major health problem in India contributing to high maternal and child morbidity and mortality. To combat this problem the Ministry of Health & Family Welfare, Government of India initiated the National Nutritional Anaemia Prophylaxis programme (NNAPP) in 1970 to provide iron and folic acid supplements to pregnant women, lactating women, family planning acceptor women and children between the age of 1 and 11 years. Number of studies done, therefore in different parts of India revealed that the problem is still continuing without any significant decrease. The ICMR then therefore, conducted an independent evaluation of the NNAPP in 1985-86 in 11 states using multicentre task force approach. The study revealed that the programme had not been well implemented. The number of beneficiaries estimated from the population surveys and the birth rates was much higher

It was in the late 1950s, when I met Dr. Gopalan first time. The most admirable thing in Dr. Gopalan was his attention to detail, lust for work and life and a global futuristic view of science in which all knowledge was integrated. His grasp of the science of nutrition and its relationship to other biological sciences is well known and widely recognized.

*Pushpa M Bhargava*

than the target to be covered and fixed by different States. The beneficiaries who have actually received the supplements were far less than the numbers shown in the records. The quality of the tablets was found to be very poor on analysis. The knowledge of functionaries and beneficiaries was much lower than the desired level. The educational component of the programme had not received adequate attention. The haemoglobin level was not found to be significantly different between beneficiary and non-beneficiary groups.

The findings of the study were discussed. One likely reason for this poor performance of NNAPP was the dose of the supplement for pregnant women then being used in the programme i.e 60 mg of elemental iron with 500 µg of folic acid given daily. The ICMR's Task Force on Nutritional Anaemia therefore recommended that a trial be undertaken in pregnant women using different doses of iron (60, 120 and 180 mg) given daily under actual field conditions i.e. where intake of supplements is unsupervised, on a multicentre basis. The results of this six-centre study (1987-89) indicated that the dose of 120 mg iron with 500 µg of folic acid given daily is probably the optimum dose under actual field conditions considering both the efficacy reflected by rise in haemoglobin, as well as the clinical side-effects in the users. The interim results of this study had been discussed by a Scientific Expert Group of the Ministry of Health & Family Welfare in 1989. Based on the results of this study and experiences gained elsewhere in the world, the dose of iron then had been increased from 60 mg to 100 mg daily and the programme was redesignated as the National Anaemia Control Programme in 1991.

The ad-hoc surveys carried out on goitre/IDD and the clinical impressions in different parts of India strongly indicated that iodine deficiency disorders are not only restricted to the mountainous and hilly areas of the Sub-Himalayan range but are also prevalent in many other regions of different geographical characteristics. The "Extra-Himalayan Foci" where these studies were conducted had no similarities regarding geographical and meteorological characteristics, food and living habits of the affected population. The endemic areas were located in plains, mountains, riverine areas and plateaux, and the affected populations were both tribals and non-tribals with significantly differing dietary habits. It was strongly felt that before the universal iodation of salt programme goes into full operation, more information regarding the prevalence of iodine deficiency disorders in different regions of India with different geographical characteristics should be made available to the planners and decision makers. The Sub-Himalayan region as the only affected region in the country with higher priority for receiving iodated salt and treating the rest of the country, as non-endemic with lower priority would be improper. It was therefore decided by the ICMR, in consultation with the Ministry of Health & Family Welfare, to conduct a study in different parts of India to assess the prevalence of iodine deficiency disorders in different age

groups of the population and to identify other underlying etiological factors like staple food and drinking water. The study was carried out between 1983-86.

Iodization of salt is the cheapest and most convenient method to tackle the problem of iodine deficiency disorders (IDD). However, for this strategy to be effective it is essential that the average consumption of salt per person per day should be around 10 grams. It was therefore felt essential to conduct a

I first met Dr. Gopalan when I was a fresh medical graduate. Dr. Gopalan is a great visionary, an able administrator, institutional builder and a strict disciplinarian. His patriotic spirit and confidence in the scientists of the country to lead nutrition science to the forefront has helped to sculpt the entire nutritional science scenario in the country. He is a pragmatic planner who is internationally reputed and acclaimed for his forthright views on the nutritional problems of developing countries.

*Kamala Krishnaswamy*

study to assess the salt consumption pattern, including the storage and transportation of salt. The study therefore was carried out in 1987-88 in the three major seasons in different parts of India. The study has shown that the average salt consumption per adult per day is 13.8 gms with a range of 7 to 26 gms in the different states, which is higher than the generally assumed figure of 10 gms per adult per day. The average requirement of iodine for normal functioning of the body is around 150µg which means that a level of iodination of 15 parts per million at consumer level as this would provide 150 µg through the salt itself.

I came to know about Dr Gopalan in 1965 when I was looking for a job in India while in the US, and was advised by Late Prof. PS Sharma to write to Dr. Gopalan at NIN, Hyderabad. I found in Dr. Gopalan a brilliant scientist with analytical mind. He always encouraged his juniors and recognized their good ideas as well as gave them freedom of work, once convinced. Dr. Gopalan molded NIN into an interdisciplinary institution with strong departments of biochemistry, analytical chemistry, clinical nutrition, field studies and food and drug toxicology. He started the National Nutrition Monitoring Bureau, which has been generating periodically nutrition profile data, being used by policy makers and programme managers. Work done under his guidance on nutritive values of Indian foods has become a Bible. Research carried out under the guidance of Dr. Gopalan has helped to focus on protein calorie malnutrition rather than protein malnutrition. Many still harp on the latter.

*Mahtab S. Bamji*

### **District nutrition project**

There might not be any large level study where three micronutrients viz. iron, iodine and vitamin A have been studied together in a community with statistically adequate sample size. ICMR undertook a multicentre study "District Nutrition Project" in 16 districts from 11 states of the country (1997-2001). The objectives were to assess the magnitude of micronutrient (iron, iodine and vitamin-A) deficiency disorders as well as protein energy malnutrition and to develop a need based service delivery intervention model through the existing district health system. The districts were mainly covered from northern, eastern and northeastern states of the country. Besides

carrying out this big micronutrients deficiency disorder survey, the study could successfully demonstrate evidence and need-based intervention for reducing the prevalence of clinical vitamin A deficiency in Gaya district of Bihar and anaemia among pregnant and adolescent girls in Dibrugarh district of Assam. The reduction of anaemia among adolescent girls was more creditable as it was based on social marketing.

The ICMR has been carrying out extensive work on primitive tribes of India since 1999. The council has demonstrated that by empowering the community and their active participation can improve their health status and can also reduce morbidity and mortality. The project has shown that the link persons between community and health and other related systems, if used effectively, can deliver the goods for better health of these primitive tribe groups. The study has also demonstrated the concept of 'corpus funds' for sustaining the research project activities, once it is withdrawn after its tenure.

I have read his views on maternal and child nutrition during my post graduation. I met him and worked with him during his tenure as DG, ICMR. He showed that lab, clinical and operational research can help building the national policies, and can help in formulation of national programmes for combating major nutritional problems.

*Prema Ramachandran*

### **Studies in the northeastern region**

North East region of the country is priority of ICMR for nutrition research. Extensive surveys have been carried out by ICMR in last two decades to assess the nutrition profile in different age groups of population. Currently a large nutrition survey is being carried out to assess the haemoglobin, ferritin, B12, folic acid, serum retinol, zinc, selenium, vitamin D, parathormone (PTH), calcium, phosphorous and alkaline phosphate in children 6 - 71 months and pregnant mothers.

### **Surveillance of food contaminants and adulterants**

ICMR as an extra mural activity carried out extensive work on Surveillance of food contaminants and adulterants during 1985-95 in different parts of the country to assess the magnitude of the problem of contamination and adulterants. Food contaminants studied were pesticide residues (HCH, DDT and melathion); heavy metals (lead, arsenic, cadmium, copper, zinc, tin and mercury); mycotoxins (aflatoxin B1) in wheat, rice, bovine milk, fish, turmeric, and infant formula and canned fruit products samples. Similarly "surveillance of permitted and non-permitted food colours was carried out in hard boiled sugar confectionary and Ice candy as well as Crushed Ice samples" collected from different parts of India. These studies have helped the policy makers to take corrective measures.

Many more task force studies through extra mural mode viz. clinical and sub clinical vitamin A deficiency among pre school children, women's work load



and child survival linkages in slums of Delhi and Mumbai, iodine loss during cooking etc have been carried out in recent past.

ICMR through intramural and extramural research has contributed significantly in creating nutrition database, evaluation of Government programmes, developing different intervention models and carrying out basic research to enhance existing knowledge in the field.

ICMR's research work emphasized the importance of growth monitoring for early diagnosis and appropriate management of protein energy malnutrition. Growth norms for Indian children were established. Database on nutritive values of over 650 Indian foods was generated, which is used by various national organizations, planners, policy makers and programme managers. Recommended Dietary Allowances (RDA) for Indians were formulated and Food based Dietary Guidelines for Indians were also developed. Assessment of dietary intake of individuals, households and nutritional profiles of different communities has been carried out through periodic surveys of NNMB in 10 states since 1972. ICMR was instrumental in developing national prophylaxis programme against blindness due to vitamin A deficiency and in formulation of national anaemia prophylaxis programme to supplement IFA tablets to pregnant and lactating women and pre-school children. Our research demonstrated beneficial effects of commonly consumed spices such as Fenugreek seeds as dietary adjuvant for the management of diabetes and hyperlipidaemia and turmeric in chemoprevention of cancer. ICMR developed simple methods to estimate aflatoxin contaminants in food grains at field level, simple methods for removal of neurotoxin in *Lathyrus sativus*, simple and

**Dr. Gopalan as Director, National Institute of Nutrition (NIN), Hyderabad  
(1960-1974)**

Dr. C. Gopalan took over as the Director of Nutrition Research Laboratory in 1960. The Nutrition Research Laboratory was then, a small institute with barely half-a-dozen scientists. Within a period of ten years, he built up the Institution into a strong centre of Nutrition Research and Education. The Institute gained international importance, where hundreds of scientists not only from India, but also from South East Asian countries were trained in the field of Nutrition Sciences. His contribution is enormous. However, 'recommended dietary allowances' and 'nutritive values of Indian foods' as well as initiation of National Nutrition Monitoring Bureau were valuable contributions.

**Dr. Gopalan as Director General, ICMR  
(1974 -79)**

The WHO-ICMR unit in Genetic Control of Mosquitoes was terminated and the Vector Control Research Centre was established at Pondicherry. ICMR took over the Central Jalma Institute for Leprosy at Agra, which was established by the Japanese Leprosy Mission for Asia (JALMA) in 1967. The division of Information and publication was established in ICMR Headquarters. Medicinal plants of India (volume I) were published. The Malaria Research Centre was established at Delhi. The Food and Drug Toxicology Research Centre was established at the NIN Campus in Hyderabad. The Institute for Researches in Medical Statistics (Delhi and Madras Chapters) were established. An All-India Talent Search Scheme had been initiated and nearly 100 talented young medical men representing the cream of young talents of the country had been inducted into research career. Apart from permanent institutes of the Council, "Centre of Excellence" is identified in different parts of the country and ICMR research support was extended to them.

sensitive biochemical indicators for assessment of vitamin nutriture and aetiopathogenic mechanisms of various nutritional deficiency syndromes and technology of fortification of salt with Iron and Iodine for prevention of IDA and IDD. ICMR helped the Government in modifying/revising/developing guidelines for national programmes of IFA supplementation to pregnant and lactating mothers and children; Vitamin A solution supplementation to pre school children and guidelines for IDD survey. Guideline for Genetically Modified food research was also developed. ICMR has excellent center for breeding and supply of pathogen free animals to various research institutes for experimental research. We have also established a state of the art primate facility. Extensive work has been done on dissemination of nutrition messages to various vulnerable groups in the community and has been providing need-based education and training to health professionals. ICMR has trained over 1600 health professionals from 35 countries and have published over 3000 scientific publications in peer-reviewed national and international journals.

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# PROBIOTICS IN GUT DISORDERS: DO THEY WORK?

Gopalan S

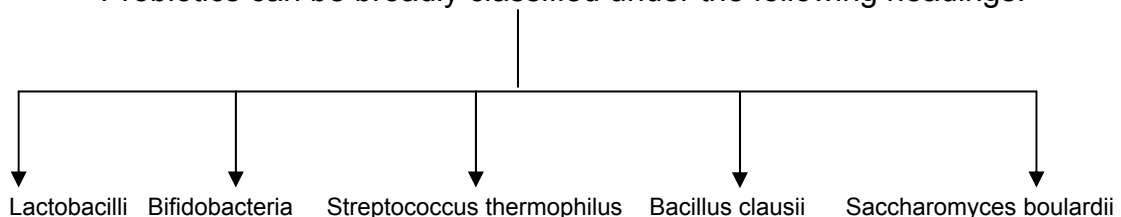
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## Introduction

With the adoption of vigorous “child survival strategies” including oral rehydration, infant and child mortality in India has significantly declined even among the poorest undernourished segments of the population. Most of the surviving children however continue to remain stunted and undernourished and fail to thrive currently 52% of India’s under-fives are stunted<sup>1</sup>. Dietary deficiencies in children of the poor are often aggravated by frequent diarrheal episodes, which are common in the unhygienic environment. Apart from nutrient losses in such diarrheal episodes, the effects of repeated gastrointestinal infections on the structure and function of intestinal villi and the resultant possible deleterious effects on nutrient absorption could also be expected to be minimized with probiotic supplementation. Among the components likely to be used in functional foods, prebiotics and probiotics are already used as food ingredients. Probiotics are “viable microbial food supplements which beneficially influence the health of human’s<sup>2</sup>. A prebiotic is a non-digestible food ingredient that beneficially affects the host by selectively stimulating the growth and/or activity of one or limited number of bacteria in the colon that have the potential to improve host health<sup>3</sup>.

The bacterial genera most often used as probiotics are lactobacilli and bifidobacteria. They can be given in the form of fermented foods such as curd, yogurt that may briefly establish in the gut. A number of health-related effects of probiotics are documented such as alleviation of lactose intolerance, decreasing the duration of rotavirus diarrhea, prevention of recurrence of superficial bladder cancer. Each effect has been shown in at least two human clinical studies by different research groups. Colonic fermentation has been shown to be altered following probiotic intake, either as fermented milks or freeze dried cultures<sup>4, 5,6</sup>. Lactobacillus acidophilus therapy in the prevention and as adjuvant therapy of certain infectious diseases especially gastrointestinal disorders in children and adults is advocated in many parts of the world. The recent emphasis on supplementation with lactobacilli is largely attributed to information obtained regarding the beneficial effects of lactobacilli in preventing or minimizing the severity of antibiotic-associated diarrheal episodes<sup>7</sup>.

Probiotics can be broadly classified under the following headings.



Probiotics have the following characteristics:

- they maintain microbial milieu to the host's advantage;
- decrease load of pathogenic bacteria;
- they are resistant to gastric acid, bile and digestion;
- they have the ability to adhere to and colonize the gut.

Some of the "Health Benefits" claimed for Probiotics, are listed below:

- nutritional enhancement: Yoghurt contains a significantly higher concentration of folic acid, niacin and riboflavin than milk.
- control of Intestinal disorders
  - Rotavirus diarrhea
  - Colitis
  - Lactose intolerance
  - Salmonella and shigella infection
- control of Other disorders
  - Ethanol induced liver disease
  - Cancer of the colon
  - Hypercholesterolaemia
- other Uses:
  - Treatment of food allergies
  - Adjuvant for vaccines
  - Increased weight gain during development

The potential mechanisms of probiotic action are:

- competing for nutrients.
- competing for receptor (adhesion) sites.
- acidification
- production of inhibitory substances (bacteriocins)
- immunomodulation (increases IgA levels)

Acute infections of the gut are usually self-limiting, characterized by diarrhea and often vomiting. Acute diarrhea is responsible for 3-4 million deaths annually worldwide, many of which are children, it accounts for 20-30% of all mortality.<sup>8, 9</sup> Several studies by different groups in developed and developing countries<sup>10, 11</sup> have shown that some probiotic lactobacilli significantly shorten the duration of rotavirus diarrhea.

A number of probiotics have been added to animal feeds to increase the weight of domestic animals. The increase in weight gain presumably results from infection control and from increased digestibility of nutrients. Animal feeding studies in young rats<sup>12,13</sup> fed a liquid diet consisting either of milk, yogurt, or fermented milk have shown a significantly higher weight gain for the animals on the fermented products. In four weeks the animals fed milk gained 116g. 136.3g when fed yogurt and 131.3g when maintained on fermented milk diet. A similar study has been conducted in humans<sup>14</sup>. From a number of different types of observations, evidence has emerged that probiotics are beneficial in promoting growth in young animals and humans.

## Lactobacilli

The use of lactic acid producing bacteria in foods, especially members of the genus *Lactobacillus*, in foods has a long history and most strains are considered commensal microorganisms with little or no pathogenic potential. Their ubiquitous presence in intestinal epithelium and the human gastrointestinal tract and their traditional use in fermented foods and dairy products attest to their safety, and are generally recognized as safe<sup>15,16</sup>. Most probiotics have been designated as 'generally recognized as safe' (GRAS). The word "lactobacillus" by itself is meaningless. Lactobacilli differ widely in their potency and this is also dependent to a great extent on both the species and host.

'Curd' is a food item, which is relatively easy to prepare and is consumed in small amounts even by poor communities in India. Curd contains several lactobacilli in varying proportions, predominantly *Lactobacillus bulgaricus*. This poses a practical problem in assessing the potency of a particular species of *Lactobacillus* in the food item from the standpoint of a possible beneficial effect in decreasing diarrheal morbidity as it is difficult to attribute the positive effect to a specific species of *Lactobacillus* in such a mixture. The composition of probiotics in curd vary considerably from region to region and may include a number of organisms such as *Leuconostoc*, *Mesenteroides*, *Streptococcus thermophilus*, *Lactobacillus bulgaricus* and *Lactobacillus acidophilus*.

From the evidence available till date, it appears that *Lactobacillus GG* is the most potent among the lactobacilli in decreasing the incidence of diarrheal morbidity. Unfortunately, a major limitation in using *Lactobacillus GG* in the developing countries is the cost factor. *Lactobacillus acidophilus* is readily available in the developing countries and activated cultures of the same can be used as probiotic food supplements. The acidophilus strain is more feasible from the economic standpoint in the developing world but does not appear to be as potent as *Lactobacillus GG* in its beneficial effect on diarrheal morbidity. Insufficient viability and survival of *Lactobacillus acidophilus* in commercial food products remains a problem. The minimum concentration of *Lactobacillus acidophilus* required to exert a possible beneficial effect on diarrheal morbidity is  $10^8$  organisms/gm of probiotic supplement.

*Lactobacillus GG* is available commercially as capsules for oral administration but the cost is inordinately high which does not make large-scale supplementation of *Lactobacillus GG* in the community feasible in the Indian context. An interesting species of *Lactobacillus* that has recently been demonstrated to have a number of beneficial effects in gastrointestinal disorders such as chronic constipation, short bowel syndrome, antibiotic associated diarrhea and even in clinical situations other than gastrointestinal disorders such as bladder cancer is *Lactobacillus casei* – more specifically the Shirota strain.

Most studies on possible beneficial effects of probiotics on diarrheal morbidity using various strains of lactobacilli till date involved supplementation carried

out over a relatively short period (several days to few weeks) and were hospital-based. This may be too short a period to document appreciable changes in the growth profile. In these studies, the probiotics were supplemented only after the onset of a diarrheal episode. Some of the studies have shown a definite role of Lactobacilli in decreasing diarrheal morbidity whereas others have not been able to demonstrate a clear benefit of probiotic supplementation in the community.

### **Bacillus clausii**

*Bacillus clausii* is probiotic, which has aroused considerable interest among clinicians and academicians in recent years. It has been demonstrated to be useful in acute diarrhea, antibiotic associated diarrhea and clostridium difficile *enterocolitis*.

### **Saccharomyces boulardii**

*Saccharomyces boulardii* is a yeast (fungus). The principle indications of *Saccharomyces* usage are based upon a large number of clinical trials, and are as follows:

- acute infectious diarrhea (esp. in infantile diarrhea as an adjunct to oral rehydration)
- chronic diarrhea (esp. Giardiasis)
- antibiotic-induced diarrhea and pseudomembranous colitis (*Clostridium difficile*)
- irritable bowel syndrome associated diarrhea.
- diarrhea in tube-fed patients
- crohn's disease

### **Clinical trials on probiotics in India**

There are some issues which have been raised in the context of probiotic supplementation in the developing countries of South Asia including India such as paucity of evidence from this part of the world regarding possible benefit of probiotic supplementation in humans and the likelihood that microbial colonization of the gut in individuals from countries like India who are exposed to a more microbiologically hostile environment as compared to the Western world may be considerably different from their Western counterparts. Furthermore, the possible benefit from a probiotic preparation is dependent on specificity of the strain as well as the host response and these may differ in the two settings.

All the published studies from India have involved probiotic supplementation only in diarrheal disorders both acute and persistent diarrhea. The randomized controlled double blind clinical trails involving probiotic supplementation in humans in India till date are briefly described below.

## Randomized controlled double blind trials

### Completed studies

- efficacy of Tyndalized *Lactobacillus acidophilus* in Acute Diarrhea.
- efficacy of *Lactobacillus rhamnosus* GG in acute watery diarrhea of Indian children: A randomized controlled trial.
- efficacy of L
- actobacillus rhamnosus GG in persistent diarrhea of Indian children: A randomized controlled trial.
- feasibility studies to control acute diarrhea in children by feeding fermented milk preparations Actimel and Indian “dahi”.
- efficacy of milk fortified with a probiotic Bifidobacterium lactis (DR-10) and prebiotic galacto-oligosaccharides in prevention of morbidity and on nutritional status.

### Efficacy of Tyndalized *Lactobacillus acidophilus* in acute diarrhea

This study was carried out at the JN Medical College, Aligarh Muslim University<sup>17</sup>. It was a hospital-based study and was randomized, placebo controlled and double blind. A total of 98 subjects with a wide age range (6 months – 12 years) were randomized to receive either (lactrol, Raptakos) 15 billion tyndalized *Lactobacillus acidophilus* (n=48) or puffed rice powder (n=50) which served as the placebo. Children with Acute Watery Diarrhea admitted to the Diarrhea Unit at JN Medical College, Aligarh were enrolled in the study. Children with systemic infection, encephalopathy, convulsions and those with a history of ingestion of commercial probiotic preparations previously were excluded. Recovery was defined as passage of 3 consecutive formed stools or no passage of stool in the previous 12 hours, whichever was earlier.

#### Text Box 1: Efficacy of Tyndalized *Lactobacillus acidophilus* in Acute Diarrhea

##### Results

Primary Outcome measure (mean duration of diarrhea)- comparable in both groups

Secondary Outcome measures -slightly less in LA group but not statistically significant-dropout- 4-treatment failure:4 (all in LA group, none in Control group)-rotavirus-14/22, V.cholerae-8/98

Conclusion: No significant benefit

Possible reasons:

- small sample size
- moderate to severe diarrhoea in these subjects, not mild diarrhea
- effects of probiotics based on colonization-? May be longer duration of supplement necessary

The study showed that the primary outcome measure which was mean duration of diarrhea was comparable in the groups (Text box 1).

Treatment failure in this study was defined as

need for intravenous fluids for more than 72 hours for correcting dehydration. There were 4 dropouts and 4 treatment failures (all treatment failures were in the group which received *Lactobacillus acidophilus*, there were none in the placebo group). For logistic reasons, rotavirus could be tested in only 22 of

the 98 subjects and was detected in 14 out of these 22 subjects tested for rotavirus.

The investigators concluded that tyndalized *Lactobacillus acidophilus* supplementation showed no significant benefit in children with Acute Watery Diarrhea. The possible reasons suggested by them were small sample size, these subjects had moderate to severe diarrhea (not mild diarrhea as in subjects from the developed countries in the West where several published studies involving probiotic supplementation in children with diarrhea were conducted) and with increased severity of diarrhea, a possible mild beneficial effect may not be appreciated. It is also well known that the possible beneficial effects of probiotic supplementation are dependent on colonization of the gut- it could well be that a longer duration of probiotic supplementation may have shown a clear benefit.

***Efficacy of Lactobacillus rhamnosus GG in acute watery diarrhea of Indian children: A randomized controlled trial***

This clinical trial was a randomized controlled double-blind hospital-based study carried out at the North Bengal Medical College and Hospital, Darjeeling<sup>18</sup>. A total of 684 children visiting the hospital who fulfilled the criteria for Acute Watery Diarrhea were randomized to receive either 60 million organisms of *Lactobacillus rhamnosus* GG (probiotic arm) along with ORS (oral rehydration solution) or ORS alone (control arm). The administration was carried out for a minimum period of 7 days or till diarrhea ceased. The primary outcome measures were decrease in frequency of both diarrhea and vomiting. The secondary outcome measure was reduction in duration of hospital stay. Children with any systemic illness other than diarrhea on admission, those who developed any systemic complication of diarrhea during hospital stay and those subjects whose families failed to give informed consent were excluded.

<b>Table 1: Efficacy of <i>Lactobacillus rhamnosus</i> GG in acute watery diarrhea of Indian children: A randomized controlled trial</b>			
	Mean±SD on Day 1	Mean ±SD on Day 7	Significance
Daily frequency of diarrhea	22.4±5.3 vs 24.1±5.8	2.0±1.2 vs .2.1±0.8	NS
Daily frequency of vomiting	6.2±2.1 vs .7.1±2.4	2.1±0.8 vs 2.0±1.2	NS
Mean Duration of diarrhea (days) 6.8±2.1vs. 6.6±2.3 NS Mean Duration of vomiting (days) 3.2±1.1vs. 3.3±1.2 NS Rotavirus identified in 490 /684(76%)-241 cases (74.6%) vs. 249 controls (77.1%)			

The results of this study (Table 1) showed that there was no significant difference in both mean duration of diarrhea and the mean duration of vomiting between the groups. Rotavirus was identified in 490 out of the 684 subjects enrolled.

***Efficacy of Lactobacillus Rhamnosus GG in persistent diarrhea in Indian children – A randomized controlled trial***

This was also a hospital –based study carried out at the North Bengal Medical College and Hospital by the same investigators who performed the study on



children with acute watery diarrhea<sup>19</sup>. A total of 235 subjects who fulfilled the definition of persistent diarrhea were randomized to receive either 60 million organisms of *Lactobacillus rhamnosus* GG along with ORS (probiotic arm, n=117) or ORS alone (control arm, n=118). The same exclusion criteria that were employed for the study by the same investigators using the same probiotic in subjects with acute watery diarrhea were also applicable to this study. The primary as well as the secondary outcome measures were the same. The results clearly showed that in contrast to the results of the study on subjects with acute watery diarrhea, *Lactobacillus rhamnosus* GG significantly decreased the mean duration of diarrhea (5.3 vs. 9.2 days) in subjects in the probiotic arm as compared to the controls from which the investigators inferred that *Lactobacillus rhamnosus* GG at a dosage of 60 million organisms administered for a minimum period of 7 days or till diarrhea ceased along with ORS could decrease frequency and duration of diarrhea and vomiting and reduced duration of hospital stay in children with persistent diarrhea.

**Feasibility studies to control acute diarrhea in children by feeding fermented milk preparations “ Actimel” and Indian “dahi”**

This study was carried out by the Departments of Pediatrics and Community Medicine at the University College of Medical Sciences, Guru Teg Bahadur Hospital, Delhi<sup>20</sup>. The objective was to study feasibility of diarrhea control in children 6 months to 5 years of age with acute diarrhea by feeding fermented milk preparations. The study had a randomized controlled double blind design and the primary outcome was the number of days taken to control diarrhea. The study was partly carried out in a hospital setting and partly in the community. A total of 150 subjects were enrolled – 75 were from the hospital (h) and the remaining 75 were from the nearby slum cluster (c) whose inhabitants periodically visited the hospital for medical treatment.

<b>Table 2: Feasibility studies to control acute diarrhea in children by feeding fermented milk preparations Actimel and Indian ‘dahi’</b>	
Arms	Assigned Intervention
Actimel arm (n <sub>h</sub> =23, n <sub>c</sub> =25)	Actimel, fermented milk containing (per gram) 10 <sup>8</sup> each of <i>Lactobacillus casei</i> DN-11400, <i>Lactobacillus bulgaricus</i> and <i>Streptococcus thermophilus</i>
Indian Dahi (n <sub>h</sub> =27, n <sub>c</sub> =25)	Indian Dahi (Lf40) containing (per gram) 10 <sup>8</sup> each of <i>Lactococcus lactis</i> , <i>Lactococcus lactis cremoris</i> and <i>Leuconostac mesenteroides cremoris</i>
Ultra-heat-treated yoghurt (UHY) (n <sub>h</sub> =25, n <sub>c</sub> =25)	Ultra-heat-treated yoghurt preparation (no live bacteria)

The 75 subjects in each of the settings were randomized into 3 groups (Table 2) – the first received a fermented milk Actimel containing per gram 10<sup>8</sup> organisms each of *Lactobacillus casei* DN-11400, *Lactobacillus bulgaricus* and *Streptococcus thermophilus*. The second group received Indian ‘dahi’ Lf40 containing per gram 10<sup>8</sup> organisms each of *Lactobacillus lactis*, *Lactobacillus lactis cremoris* and *Leuconostac mesenteroides cremoris*. The third group received ultra-heat-treated yoghurt, which was an inert preparation. All children 6 months to 5 years of age with acute diarrhea (defined as 3 or more watery stools per day) were included and children with

any of the following were excluded – drug-induced diarrhea, Malabsorption Syndrome, persistent diarrhea, associated systemic illness, antibiotic ingestion, allergy to dairy products and children with Shigella, Salmonella or Vibrio infections were excluded.

Type	Hospital n=75			Community n=75		
	n	Mean	SD	n	Mean	SD
UHY	25	2.1	0.72	25	2.4	0.9
Indian 'dahi'	27	1.8	0.61	25	2.2	1.0
Actimel	23	1.5	0.48	25	1.9	0.8
Significance	P <0.01			P <0.05		

The results (Table 3) showed that both Actimel and Indian dahi are effective in the control of acute diarrhea, but the fermented milk preparation Actimel is superior.

***Efficacy of milk fortified with a probiotic Bifidobacterium lactis(DR 10)<sup>TM</sup> and prebiotic galacto-oligosaccharides in prevention of morbidity and on nutritional status***

The study was the outcome of collaboration between the Bloomberg School of Public Health, Johns Hopkins University, Baltimore, USA and the Centre for Micronutrient Research, Annamalai University, India and was carried out on a semi-urban population in Sangam Vihar in New Delhi<sup>21</sup>. It was a randomized double-blind placebo-controlled preventive efficacy study. The primary outcome was reduction in incidence of diarrhea and dysentery. The secondary outcomes included reduction in prevalence of severe illness days, days with fever, prevalence of ear infections, and reduction in incidence of iron-deficiency anemia and improved nutritional status. A total of 634 subjects were enrolled (Text Box 2) and randomized to receive either a milk fortified with probiotic and prebiotic (n=317) or unfortified milk(n=317). The inclusion criteria were children between 1 and 3 years of age at enrollment, residents of the specified locality and likely to remain in the same area for the next one year and children of parents consenting to participate in the trial. Children with

**Text Box 2: Efficacy of Milk Fortified with a Probiotic Bifidobacterium lactis (DR10)<sup>TM</sup> and Prebiotic Galacto-Oligosaccharides in Prevention of Morbidity and on Nutritional Status**

Supplementation with PP milk resulted in significant reduction in incidence of dysentery (OR 0.78, 95% CI 0.61,1.00) as well as prevalence of dysentery (OR 0.85, 95% CI 0.71, 1.01) reduction in incidence of diarrhea (10%) with PP milk not statistically significant. PP milk supplementation caused significant reduction in prevalence of severe illness days(OR 0.84, 95% CI 0.74 – 0.95, p< 0.001), days with fever(OR 0.68, 95% CI 0.54 – 0.84) and prevalence of severe ear infections(OR 0.93, 95% CI 0.87 – 1.00) there was 35% reduction in incidence of iron-deficiency anemia in PP milk supplemented group even when both groups were receiving isocaloric diets with the same iron content. at the end of 12 months of supplementation, PP milk supplemented children had better Z scores for WAZ(mean diff. 0.22, 95% CI 0.02 – 0.41, p = 0.03) and WHZ(mean diff. 0.18, p = 0.05) and higher weight gain(mean diff. 130 g, 95% CI 30 – 230, p = 0.02)

chronic illness, severely malnourished children and children known to be allergic to milk were excluded. The results of this study are summarized in Text box 2:

**Randomized controlled trials (RCT) with completion of recruitment of subject but results not published**

- Randomized controlled field trials of a probiotic to assess its role in preventing diarrhea
- A randomized double-blind placebo-controlled trial to assess the efficacy of a probiotic preparation VSL#3 versus placebo to induce remission of exacerbation in patients with mild and moderate (not severe) Ulcerative Colitis
- A randomized double-blind placebo-controlled cross-over study to assess the efficacy of a probiotic preparation VSL#3 versus placebo in pediatric patients with Irritable Bowel Syndrome (IBS)

S.No.	CLINICAL SETTING	PROBIOTIC STRAIN (S)	PURPOSE	RESULT
1.	Acute watery diarrhea	L. acidophilus	Treatment	No benefit
2.	Acute watery diarrhea	L. rhamnosus GG	Treatment	No benefit
3.	Persistent diarrhea	L.rhamnosus GG	Treatment	Benefit
4.	Acute diarrhea	L.Casel DN-11400,L. bulgaricus, S.thermophilus, Lactococcus lactis, Lactococcus latis cremoris, Leuconosta mesenteroides cremoris	Treatment + Prevention	Benefit
5.	Morbidity	B.Lactis (DR-10)	Prevention	Benefit
6.	Neonatal sepsis	L.plantarum	Treatment	Not yet available
7.	Ulcerative Colitis	VSL#3	Treatment	Not yet available
8.	Pediatric Irritable Bowel Syndrome	VSL#3	Treatment	Not yet available
9.	Acute diarrhea	Yakult	Prevention	Not yet available

**Concluding comments**

Till date, there has been no study conducted to compare one probiotic with another and no clear recommendations are available for probiotic use. However, beneficial effects have been observed in recurrent Clostridium difficile diarrhea, antibiotic-induced diarrhea and rotavirus diarrhea. Potential benefits may be obtained in traveller’s diarrhea, allergic colitis, AIDS related diarrhea and necrotising enterocolitis. It may be appropriate to infer that the most practical approach towards obtaining the maximum possible benefit of probiotic supplementation among poor communities in India would be to devise a method to incorporate the probiotic in the daily diet of the local community. It should also conform to the food habits and cultural beliefs of the community. This would be easily acceptable and also cost-effective. At this stage, a much larger number of studies are needed which involve probiotic

supplementation over a longer duration. This may help us in understanding and deciding the specific settings where probiotic supplementation is likely to be beneficial.

The studies involving probiotic supplementation in India have been conducted predominantly in children with diarrhea. There is a need for performing more studies involving probiotic supplementation in other specific clinical conditions. It is also important that studies on probiotic supplementation in individuals in developing countries like India should enroll a larger number of subjects and be conducted in different regions of the country.

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# **IRON DEFICIENCY ANAEMIA IN INDIA SOME CONTROL STRATEGIES FOR SCHOOL CHILDREN AND PLANTATION WORKERS**

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## **Introduction**

Iron Deficiency Anaemia (IDA) is the most widespread disorder among all population segments in India. Strategies for IDA control in school children participating in the mid-day meal programme, and for women tea pluckers on a tea estate are described in this paper.

## **IDA control by addition of health package to the ongoing mid day meal programme in Gujarat**

Children cannot benefit fully from primary education unless they are in a satisfactory state of health. It is particularly important that they should be well nourished and free of diseases associated with deficiencies of iron, iodine and Vitamin A<sup>1-13</sup>. Since August 1995, 40 million primary-school children in India have been receiving a free midday meals, and it is intended that by 1997 all of the country's 160 million children in this category will be doing so. In the State of Gujarat, nearly 3 million primary-school children, who already receive a free mid-day meal; have also been given iron tablets, Vitamin A capsules and iodized salt, in addition to deworming tablets containing albendazole<sup>14</sup>. An evaluation of this initiative has been made by Tara Consultancy Services, a non - governmental organization, which works with the Partnership for Child Development, of Oxford University, UK<sup>15-19</sup>.

## ***Setting up and running the project***

Focus group interviews were conducted with government officials, teaching staff, parents and school children before treatment started, in order to assess opinions on the proposed courses of action<sup>15</sup>.

- midday meal programme officials said that most children suffered from worm infestation and nutritional deficiencies.
- many children said that they passed worms, felt tired and could not always see properly.
- parents were generally unaware of these problems.
- all interviewees responded positively to the intended programme. The teaching staff and parents said that they would help to carry out treatment.

The mid-day meal programme commissioners procured adequate supplies of albendazole tablets (400 mg), iron tablets (60 mg) and Vitamin A capsules (200 000 IU) for almost 3 million primary -school children. Iodized salt was used routinely in cooked meals. Pharmaceutical firms transported the drugs to the districts or talukas where the health officers cooperated in storing them, the officials and organizers of the mid-day meal programme collected their quotas and dosed the children for whom they were responsible as prescribed

by an expert technical committee. Procurement, delivery and receipt of the products were all conducted in a highly efficient manner.

Highly cost-effective and efficient training pyramids were established, with the chief district health officers at the top and the helpers and cooks at the base. The shelf life of the drugs exceeded two years, provided they were kept in a dry place and, in the case of Vitamin A, away from the light. In the focus group interviews, all providers and receivers enthusiastically accepted the programme<sup>16</sup>.

### **Findings and outcome**

Nearly 75% of schoolchildren in a slum area carried infections of *Entamoeba histolytica* and/or roundworms, most of them severe to moderate. Infected children in the age range of 6 - 15 years were 2 kg lighter and 3 cm shorter on average than non-infected children. The mean haemoglobin levels in infected and non-infected children were 10.4 g/dl and 11.6 g/dl, respectively. Children of ages 11 - 15 years showed a more severe depression of haemoglobin than did younger children<sup>17</sup>.

**Table 1: Impact of health inputs on the mean weight and height of 83 schoolers (6–15 years) before and after deworming and micronutrient supplementation**

Variables	Baseline	Resurvey
	Mean ± SEM	
Weight (kg)	21.9 <sup>a</sup> ± 0.56	23.5 <sup>b</sup> ± 0.58
Height (cm)	124.7 <sup>a</sup> ± 1.19	127.9 <sup>b</sup> ± 1.18

Figures having different superscript in the same row are significantly different from each other

Three thousand children in three districts were followed up from prior to initiation of the intervention up to completion of one year. It was found that older children benefited more than younger ones<sup>18</sup>.

- on average, children who received the doses of supplements were 1.1 kg heavier and 1.1 cm taller than those who did not. (Table 1).
- after one year, the mean haemoglobin level was 12.4 g/dl, whereas before treatment it had been only 10.6 g/dl (Tables 2 and 3 and Figure 1).
- the prevalence of intestinal parasitic infection fell from 71% to 39%.
- the prevalence of night blindness and ocular signs of vitamin a deficiency fell from 67% to 34%.

**Table 2: Impact of health inputs on the mean haemoglobin levels (g/dl) of schoolers (6 – 15 years) in the Baseline and Resurvey covering the three study districts**

Age groups	Baseline	Resurvey
	Mean ± SEM	
<b>6 – 10 years</b>		
Boys	10.5 ± 0.06 <sup>a</sup> (650)	11.7 ± 0.05 <sup>b</sup> (818)
Girls	10.5 ± 0.05 <sup>a</sup> (644)	11.6 ± 0.05 <sup>b</sup> (852)
<b>11 – 15 years</b>		
Boys	10.9 ± 0.06 <sup>a</sup> (581)	12.0 ± 0.06 <sup>b</sup> (623)
Girls	10.5 ± 0.07 <sup>a</sup> (601)	11.9 ± 0.06 <sup>b</sup> (626)
<b>6 – 15 years</b>		
Boys	10.7 ± 0.04 <sup>a</sup> (1231)	11.9 ± 0.04 <sup>b</sup> (1441)
Girls	10.5 ± 0.04 <sup>a</sup> (1245)	11.7 ± 0.04 <sup>b</sup> (1478)

Figures in parentheses denote sample size; Figures having different superscript in the same row, between surveys, are significantly different from each other

- many children who had received the supplements said that they felt more active than previously and that their eyesight in poor light had improved.
- children who had been infected with worms felt greatly relieved to be rid of them.

**Table 3: Impact of health inputs on the prevalence of IDA among schoolers (6 – 15 years) in the Baseline and Resurvey covering the three study districts**

	Baseline						Resurvey					
	Boys		Girls		Total		Boys		Girls		Total	
	N	%	N	%	N	%	N	%	N	%	N	%
<b>Urban</b>												
Iron – deficient	530	77 <sup>a</sup>	573	79 <sup>a</sup>	1103	78 <sup>a</sup>	408	56 <sup>b</sup>	441	57 <sup>b</sup>	849	57 <sup>b</sup>
Non Iron - deficient	115	23	151	21	306	22	319	44	331	43	650	43
<b>Rural</b>												
Iron – deficient	492	90 <sup>ab</sup>	491	94 <sup>ab</sup>	983	92 <sup>ab</sup>	317	44 <sup>bc</sup>	378	54 <sup>bc</sup>	695	49 <sup>bc</sup>
Non Iron - deficient	54	10	30	6	84	8	397	56	328	46	725	51
<b>Total</b>												
Iron – deficient	1022	83 <sup>a</sup>	1064	86 <sup>a</sup>	2086	84 <sup>a</sup>	725	50 <sup>b</sup>	819	55 <sup>b</sup>	1544	53 <sup>b</sup>
Non Iron - deficient	209	17	181	14	390	16	716	50	659	45	1375	47

IDA = < 12 g Hb/dl;  
 Figures under each matching head different superscript row, between surveys, are significantly different from each other; Figures having different superscript in the same column between urban and rural are significantly different from each other

**Figure 1: Frequency distribution of haemoglobin level (g/dl) in schoolers (6-15 yrs) in the Baseline and Resurvey covering the three study districts**

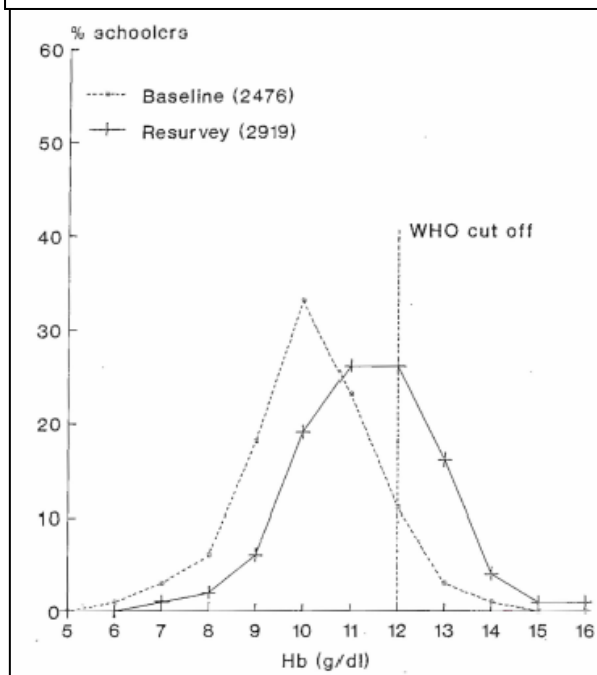


Figure in parentheses denotes sample size

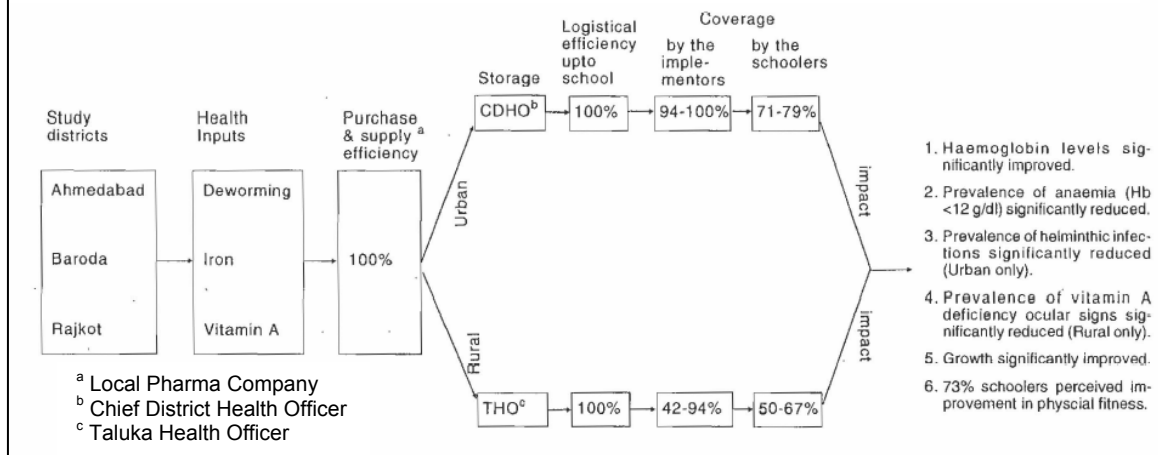
Many studies throughout the world have shown that, in general, people on low incomes suffer more from iron and vitamin A deficiencies than from inadequate calorie or protein intake, and tend to be comparatively heavily infected with intestinal parasites that greatly inhibit growth and depress levels of iron and vitamin A. Wherever iodine deficiency disorders are endemic it is essential that all people use iodized salt. Even moderate iodine deficiency can have an adverse influence on the learning process.

Deworming, and supplementation with iron and vitamin A, should be organized as parts of a single strategy. Deworming helps to maintain haemoglobin levels for

three to four months. Adequate dietary iron is needed for cognition and



**Figure 2: An overview of the delivery logistics and impact of the health package on the schoolers (6-15 years) covering the three study districts**



physical activity, while vitamin A, is vital for eye health and combats common morbidities, especially upper respiratory tract infections. Reducing these complaints also reduces absenteeism among school children.

Though the programme may seem ambitious, its financial requirements are very modest. An overview of the delivery, logistics and impact of the health package on the school children (6 - 15 years) covering the three study districts is given in Figure. 2. The annual cost per child for albendazole, iron, vitamin A and iodized salt is approximately Rs. 11 and that of midday meals is about Rs. 300. Preferably, of course, both deworming treatments and the midday meals should be given.

### **Programme implications and recommendations**

- The Integration of the school health inputs of an antihelminthic medication and micronutrients cost the Gujarat MDMP only Rs. 10.56 (US 35 cents) per child per annum. Even calculated at Rs. 15/child /year multiplied by 5 to 7 school years of primary school, this would cost only Rs. 75/- to Rs. 105/- per child for an extremely sustainable and cost-effective programme.
- Since the majority of the school children in the Government schools come from the poorer socio-economic segments, it is necessary to integrate the anti-helminthic and micronutrient package into the centrally financed mid-day meal scheme.
- Approximately Rs. 2400/- million/annum is a small price to pay to achieve a dramatic reduction in intestinal parasitic infections and the major micronutrient deficiencies in school children. Intestinal parasite control would greatly enhance growth as well as iron and vitamin A status. There is a definite synergy between adequacy of the above micronutrients and improved learning capacity. The nutritional and health impact of the mid-day meal can be enhanced manifold by the catalytic addition of the above inputs. In fact we should ask ourselves whether we could afford to deny our school children this intervention.

- The potential for a multiplier effect, with a satisfied school child going on to be a good IEC agent with his/her family, is immense and should be exploited. The school can become a strong second line of health defence for the whole community and for the entire nation.
- It is of utmost importance to cover all school children for prevention of IDA. This is crucial to ensuring the presence of actively learning children (cognition and physical capacity) in our classrooms. The national IDA Control Programme has by-passed and still bypasses this extremely vulnerable and easily accessible target population. For optimal and sustainable improvement in haemoglobin levels, it is imperative to give anti-helminthics and micronutrients to the young child.
- The improved MDM - programme of Gujarat has shown that it is feasible and cost-effective to integrate the "school health package" into the on-going MDMP.
- It is urged that the Government of India follow the "Gujarat Model" in its Centrally-sponsored MDMP Scheme for a start, at least the States and UTs that have opted for a cooked mid-day meal should go ahead with the programme.
- Even those States/UTs that have opted not for a cooked meal, but for grain distribution, can easily deliver double-fortified salt (iron and iodine) through the Public Distribution System. Bi-annual campaigns for deworming and vitamin A capsule distribution can and should be carried out regardless of whether the State/UT has opted for a cooked MDM or not.
- In short, the school child, especially the pre-adolescent/adolescent desperately requires his/her haemoglobin status to be improved. Whether this is done through supplementation, fortification or dietary means or combinations thereof, the important thing is to get the iron into the school child. These school children are going to be the parents and citizens of tomorrow.
- A satisfied school child can be the best communicator to his/her family.
- In programme terms, unless the Receivers (School children) see a real and concrete benefit in an intervention, it will not work. By way of contrast to the school children having a rather ambiguous opinion of the MDM, they were able to see concrete gains in the tablets/capsules consumed by them in terms of their better physical fitness, increased energy/activity levels, ability to study better, less tiredness, better appetite, freedom from worms etc. Such real or perceived benefits can and should be capitalized upon in IEC programmes targeted to the children, their parents, their teachers, their panchayats and their communities.

### **A multi-nutrient package for tea plantation workers for better health, productivity and profitability**

#### ***Focus and rationale***

The focus of this OMNI-ILSI funded demonstration-cum-research action project on "a multi-nutrient package for tea plantation workers for better health, productivity and profitability" was the workplace. Plantations are generally bypassed by the Government's primary healthcare system<sup>20-25</sup>. A

further focus of this research project was to work as an equal partner with the management of the tea estate and to demonstrate to them the simplicity and cost-effectiveness of the intervention. The multinutrient package consisted of iron and Vitamin A supplementation and iodized salt.

India with a total tea production of about 780 million kilograms (kg) in 1996 is the largest producer of tea in the world. It accounts for nearly 30% of the global production of tea. India also happens to be the largest consumer of tea in the world. In fact, domestic demand for tea has outstripped production despite phenomenal technological advances in increasing tea-crop yield and productivity. The same zeal, however, has not been extended to increasing human productivity although 'plucking' is a highly cost- and labour-intensive step in tea manufacture<sup>26, 27</sup>. This step of the manufacturing process accounts for most of the employee costs<sup>28-31</sup>.

### ***Objectives of the study***

- to try and reduce the 'hidden hunger' for iron, iodine and vitamin A in the entire workforce and their families on a tea estate in South India.
- to intervene for nine months with a multinutrient package of supplemental iron and vitamin A and iodized salt.
- to jointly plan and implement the demonstration-cum-research – action project with the Management of the tea estate.
- to evaluate the improvement, if any, in worker health, worker productivity and profitability (to the worker and/or to the Management).
- to evaluate whether referral to the nearby hospitals and absenteeism decreased as a result of the micronutrient intervention.
- to establish, if possible, the causal link between iron supplementation, regularity of dosing, rise in haemoglobin levels, rise in productivity and rise in monthly income among the female pluckers.
- to establish the link, if any, between increase in monthly income and increase in the intake of food energy, protein and BMI values of the female pluckers.
- to establish differences, if any, in productivity between the nine gangs of female tea pluckers and reasons for such differences Plan of action and its implementation

The plantation district of Chikmagalur is endemic for iodine deficiency disorders (IDD). It also has a high prevalence of iron deficiency anaemia (IDA); and vitamin A deficiency (VAD). The intervention package consisted, therefore, of all the three micronutrients.

### ***The study design***

The Balanoor Plantations and Industries Ltd., situated in the Chikmagalur District of Karnataka State, South Western India was our study estate. The entire workforce of 617 (pluckers and non-pluckers) and their families (approximately 2000 – 2500 individuals) were the beneficiaries of the micronutrient intervention of 9 months' duration. Three types of evaluation were conducted. These were process evaluation, impact evaluation, and cost

effectiveness evaluation. The focus of our study was directed towards the 334 female pluckers. The study design envisaged that each plucker was her own control. The pre-intervention period was from August 1995 to April 1996. The intervention period was from August 1996 to April 1997. In addition a control estate (Devon Plantations and Industries Ltd.) was included for comparison of key agricultural statistics like rainfall, crop yield (kg/hectare) and average tea plucked/per worker/per day in the corresponding pre- and during-intervention periods.

The choice of this research design was justified for the following reasons:

- The correlation coefficient (0.8077) between crop yield and average tea leaves plucked (Kg/worker/day) was highly significant at the 0.01 level, thereby indicating that it was a potent factor for productivity. The crop yield was virtually the same in the pre- and during-intervention periods at 1668 Kg/hectare and 1607 Kg/hectare, respectively. Hence, this important factor was controlled.
- The women pluckers belonged to the same gangs in the pre- and during-intervention periods. Our statistical analyses established that three out of the nine gangs were significantly superior to the others. Hence, this important factor was also controlled.

### ***The micronutrient intervention***

The micronutrients consisted of 240 mg ferrous sulphate delivering 60mg elemental iron twice a week; 1600 IU Vitamin A and 400 IU Vitamin D once a week; and heavily subsidized iodized salt (30 ppm) for daily cooking for the whole family. The medicinal supplements, consisting of 250 tablets of iron and 125 capsules of Vitamin A were put into screw-top plastic containers to last a family of 5 members for 5 months. They were handed over at the baseline survey in August 1996 to each worker; and refilled again in December 1996 to last another 5 months. The cost of the micronutrients/family/year was Rs. 61.50 or Rs. 12 per family member. Except for Vitamin A the other two inputs were available free of cost. The women were held responsible for ensuring regularity of intake of supplements by all the family members.

### ***Information education communication (IEC)***

A simple IEC sheet was developed on the dosing regimen and benefits in the Kannada language (major local language) and was distributed to the workforce and supervisors at frequent intervals throughout the intervention period. The supervisors/gang leaders were made responsible for transmitting the IEC to their workers/pluckers.

### ***The division of tasks between the study estate and Tara consultancy services (TCS, the research team)***

*What the study estate did*

- implemented the micronutrient intervention.

- procured the iodized salt and sold it at a subsidized rate of Rs. 2/- per kg. vs. Rs. 5.50/- in the open market.
- maintained the necessary registers and sent monthly reports to TCS.
- the medical officer continuously trained the implementing staff.

### What TCS did

- developed the plan of action in consultation with the CEO and Management.
- developed a simple and sustainable research design.
- oriented the CEO and Management; trained the medical/health staff.
- jointly developed the information-education-communication (IEC) in the major local language – Kannada.
- studied and made use of on-going data systems, namely, hospital registers and computerised management information systems (MIS) on crop yield, average tea plucked, attendance etc.
- collected, analyzed and interpreted primary and secondary source data.

**Figure 3:Flow diagram of the micronutrient package (iron + vitamin a + iodine) on haemoglobin levels and average tea plucked (kg) by the female pluckers over the nine months intervention**

% Receiving the Multinutrient Package		% Regularity of Use	Hb Levels (g/dl)		Average Tea Plucked/Plucker/Day (kg)				
Pre	During	During (9 months intervention)	Pre	During	Months	Pre		During	
						N	Mean	N	Mean
	August '96 to December '96 (4½ Months)	Regular 54% (N = 180)	Regular 11.1g (N = 180)	Regular 12.0g (N = 180)	August	327	25.7	315	27.4 ***
N	99% (N = 334)				September	313	24.8	322	33.6 ***
I		Irregular 44% (N = 147)	Irregular 10.9g (N = 147)	Irregular 11.8g*	October	326	29.2	315	27.6 **
L	December '96 To April '97 (4½ Months)	Stopped 2% (N = 7)	Stopped 11.0g (N = 7)	Stopped 11.3g (N = 7)	November	324	27.7	321	34.4 ***
	99% (N = 334)				December	326	22.4	315	25.9 ***
					January	313	17.3	268	16.3 *
					February	311	17.6	317	20.5 ***
					March	305	16.1	288	18.6 ***
					April	322	24.8	302	24.2 NS
	Overall 99% (N = 334)	Overall about ½ were regular	Overall 11.0g	Overall 11.9g		2857	Overall 22.9	2763	Overall 25.60 ***

Note:

- About 95% of the sample was available at both the Pre and During Intervention for calculating the Average Tea Plucked. This is reflected at (4)
  - Variation in labour employed and Average Tea Plucked is to be noted over the nine months intervention
  - Regular is defined as taking the iron supplement twice a week, Vitamin-A once a week and iodised salt daily in cooking
  - 'Stopped' is defined as not taking the iron+Vitamin-A, but used the salt.
- \*\*\* Significant at p <0.001, \*\* Significant at p <0.01, \* Significant at p <0.05, NS Not significant

## The results

### Effect on micronutrient and health status:

- Eighty five percent of the workforce received the supplements at each round; the corresponding figure for the female pluckers was 99%.
- The Hb levels improved significantly both in the female workers (from 10.8 to 12.1 g/dl) and in the male workers (from 11.6 to 14.0 g/dl). In the women pluckers it rose significantly from 11.0 to 11.9 g/dl (Figure 3).
- Clinical signs of iron deficiency reduced significantly (49% to 11%). So did the clinical signs of vitamin A deficiency (19% to 14%) and iodine deficiency (17% to 7%). (Table 4)

- Common health problems decreased significantly from 88% to 54%.
- The number of patients referred to bigger hospitals reduced significantly from 116 patients to 86.

**Table 4: Impact of the Micronutrient Intervention on clinical signs of Iron deficiency in the Pluckers, Non-pluckers and Children in the Study Estate**

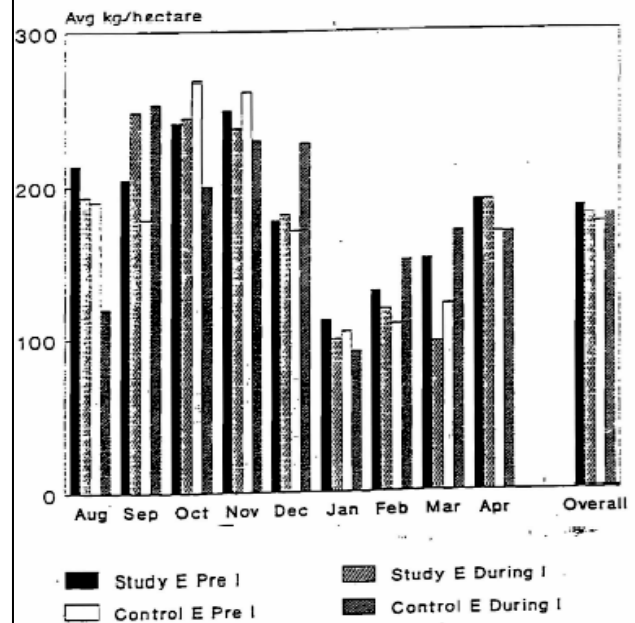
	Baseline		Resurvey	
	N	%	N	%
<b>Plucker</b>				
No sign	190	55	312	89 ***
Any sign	158	45	37	11
Pale Conjunctive	156	45	33	9 ***
Pale Nails	78	22	10	3 ***
<b>Non-plucker</b>				
No sign	141	52	242	92 ***
Any sign	128	48	22	8
Pale Conjunctive	112	42	21	8 ***
Pale Nails	81	30	2	1 ***
<b>Children</b>				
No sign	29	35	55	80 ***
Any sign	55	65	14	20
<b>Total</b>				
No sign	360	51	609	89 ***
Any sign	341	49	73	11
Comparison between Baseline and Resurvey; *** Significant at $p < 0.001$				

August, September, October and November, the moderately good

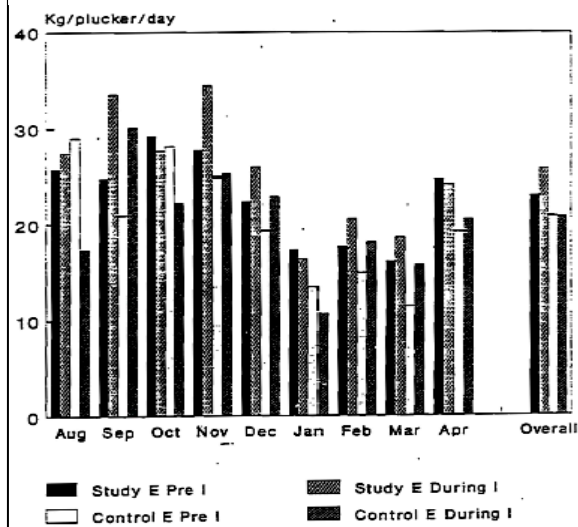
### Effect on productivity

Crop yield and average tea plucked are significantly correlated. The best crop yield months in the nine months of pre- and during -intervention were

**Figure 4: Month by month comparison of Crop yield in the Pre and During Intervention (I) periods in the Study and Control Estates (E)**



**Figure 5: Month by month average kg leaves plucked/day per plucker in the Pre and During Intervention (I) periods in the Study and Control**



crop months were December and April; and the bleak months were January, February and March. The average tea leaves plucked or worker productivity followed the same seasonal pattern. (Figures 4 and 5).

Since, 'pluckers' account for the greatest cost in tea production, the Management employs labour accordingly. The female pluckers on the permanent work force are encouraged to take leave from January to March, whereas extra temporary labour is employed in the peak crop months.

The average crop yields of the study estate in the pre- and during-intervention periods were 1668 kg/hectare and 1607 kg/hectare, respectively, and were

almost identical. Consequently this variable was controlled. The average amount of tea plucked, however, increased significantly in the study estate from 22.90 kg in the pre-intervention period to 25.60 kg in the during-intervention period. It remained stagnant at 20.80 kg and 20.69 kg in the control estate (Table 5).

**Table 5: Comparison of Average Tea Leaves Plucked (kg/Plucker/day) in the Pre and During Intervention Periods in the Study and Control Estates**

Months	Study		Control	
	Pre	During	Pre	During
August	25.7	27.4	29.02	17.33
September	24.8	33.6	20.88	30.05
October	29.2	27.6	28.07	22.11
November	27.7	34.4	24.92	25.16
December	22.4	25.9	19.29	22.87
January	17.3	16.3	13.51	10.71
February	17.6	20.5	14.99	18.06
March	16.1	18.6	12.52	15.71
April	24.8	24.2	19.22	20.54
Average	22.9	25.6*	20.8	20.69

\* indicates that the value of 25.6 was significantly better than 22.9 in the Study Estate at  $p < 0.001$  level; There was no significant difference between 20.80 and 20.69 in the Control Estate.

intervention period. Their average Hb level was 11.1 g/dl. In the intervention period, the number of good pluckers rose to 166. Their mean plucking average was 29.3 kg. Their mean Hb levels rose to 11.9 g/dl. By way of contrast there were 224 moderate pluckers (who plucked between 14 and 25 kg) and 3 poor pluckers (those who plucked less than 14 kg) in the pre-intervention period. Their average plucking rate was 19.9 kg and their mean Hb level was 11.0 g/dl. At resurvey, there were only 173 moderate pluckers and their mean plucking rate was 21.7 kg. There was only one poor plucker. The mean Hb level went up to 12.1 g/dl. Hence, the micronutrient intervention was successful in not only improving mean Hb levels but also in reducing the numbers of 'moderate' pluckers, most of whom went into the 'good' category. This was what the Management also desired (Table 6).

As per the Labour Law, a plucker has to pluck a minimum of 14 kg of tealeaves per day in order to be paid a minimum of Rs. 43/- per day. The management would rather pay an incentive of about Rs.8/- or more + Rs. 43/- per day to a 'good plucker' (who plucks more than 25 kg per day) than Rs. 43/- for borderline pluckers. All tea plantations are aiming at fewer pluckers to whom they will pay incentives. As per this categorization, there were 113 good pluckers who plucked 28.1 kg/w orker /day in the pre-

**Table 6: Impact of the Micronutrient Intervention on average Leaves Plucked (kg/plucker/day) by the Good, Moderate and Poor Pluckers and their Haemoglobin levels in the Study Estate**

Pluckers	Pre Intervention		During Intervention	
	Leaves Plucked	Hb	Leaves Plucked	Hb
<b>Good</b>				
N	113	107	166	143
Mean	28.1 ***	11.1	29.3 ***	11.9 ***
SD	2.47	0.91	3.15	1.13
<b>Moderate + Poor</b>				
N	227	227	173	137
Mean	19.9 ***	11	21.7 ***	12.1 ***
SD	3.01	0.96	2.49	1.18
<b>Overall</b>				
N	340	308	339	284
Mean	22.6	11	25.4 ***	12 ***
SD	4.79	0.94	4.74	1.16

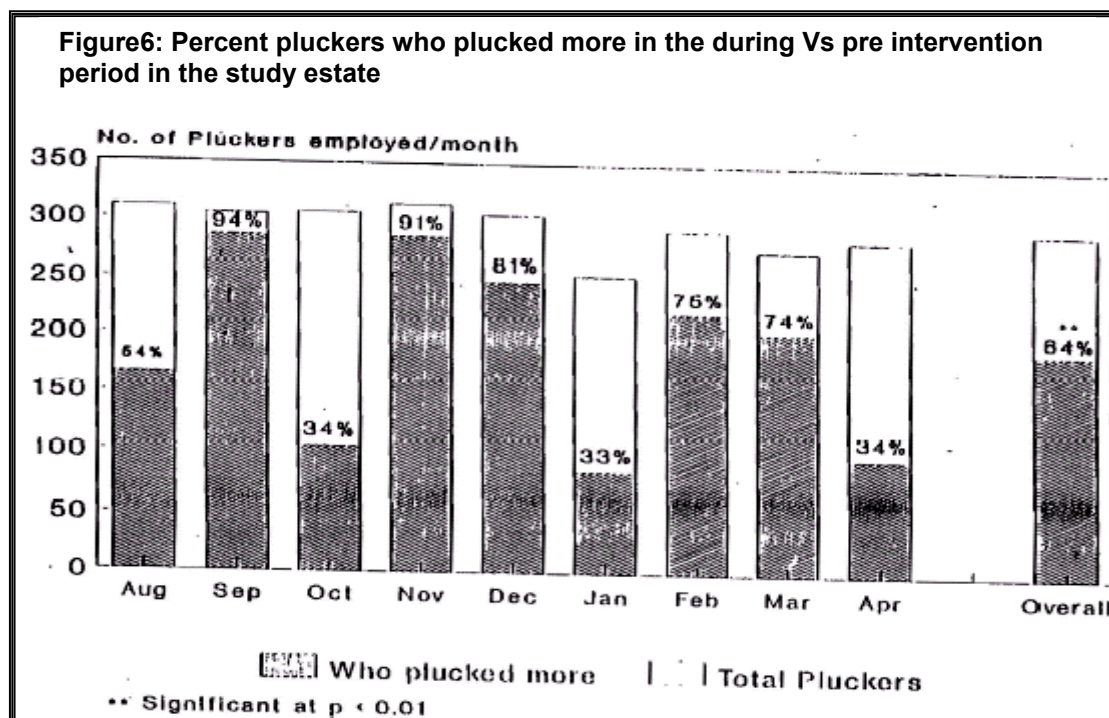
Good plucker: More than 25 kg leaves plucked per day; Moderate plucker: 14 to 25 kg leaves plucked per day; Poor plucker: Less than 14 kg leaves plucked per day; Comparisons within Pre and During Intervention periods; Good Vs Moderate + Poor kg leaves plucked; Hb levels; Comparisons between Pre and During Intervention periods kg leaves plucked; Hb levels; \*\*\* Significant at  $p < 0.001$

The number of pluckers employed decreased substantially from January to April during the 9-month-intervention-period. In all, 104 fewer pluckers were employed in the Intervention Period (2763) vs the Pre-Intervention Period (2857). The Management of tea plantations has a permanent work force and also an *ad hoc* one. They call upon the services of the *ad hoc* work force as and when needed. The *ad hoc* workers are trained pluckers and get the same wages as the permanent work force. The big difference is that they do not get free accommodation, water and electricity. The cost of labour saved was Rs. 1,11,800/- in the intervention period. Matched data of pluckers showed that 64% of them plucked more in the during-intervention period than in the pre-intervention period (Figure 6).

Absenteeism stood at a high 27% and did not change. Absenteeism is mainly due to social reasons and not due to ill health. The marriage season and important festivals such as the Harvest Festival and New Year fall in the months of January to April (Figure 7). However those pluckers who had Hb levels of 12 g/dl or more did tend to have a better attendance record of 56% (More than 20 days in a 25 work-day-month) as compared to those with Hb levels of less than 10 g/dl (43% attendance record).

#### **Effect on profitability for management and worker**

- In the intervention period, on an average 166 'good pluckers' (defined as those who pluck more than 25 Kg per day), earned about Rs. 245/- p.m. as incentive over and above the mandatory wage of Rs. 1,075/- (25 days/month). The 173 moderate pluckers (defined as those plucking between 14 and 25 Kg/day) would have earned on an average - Rs. 135/- as incentive over and above their mandatory wage. The Management has always been paying incentive wage. They paid approximately Rs 80,000/- more as incentive wage in the intervention period as compared to the pre-





intervention period. Hence, a very large proportion of the female pluckers (339) plucked more and earned more.

- The Management paid Rs. 43,000/- for the micronutrient inputs. But they appreciated the better health of their work force and the better plucking and yield results. Hence, what they saved in employing fewer pluckers (Rs. 1,11800/-) more or less set off what they paid to the good workers to pluck more and earn more.
- The additional analyses, which we did on 173 women pluckers for whom we had complete data, confirmed and strengthened what we have reported for the 334 women pluckers (Table 6).

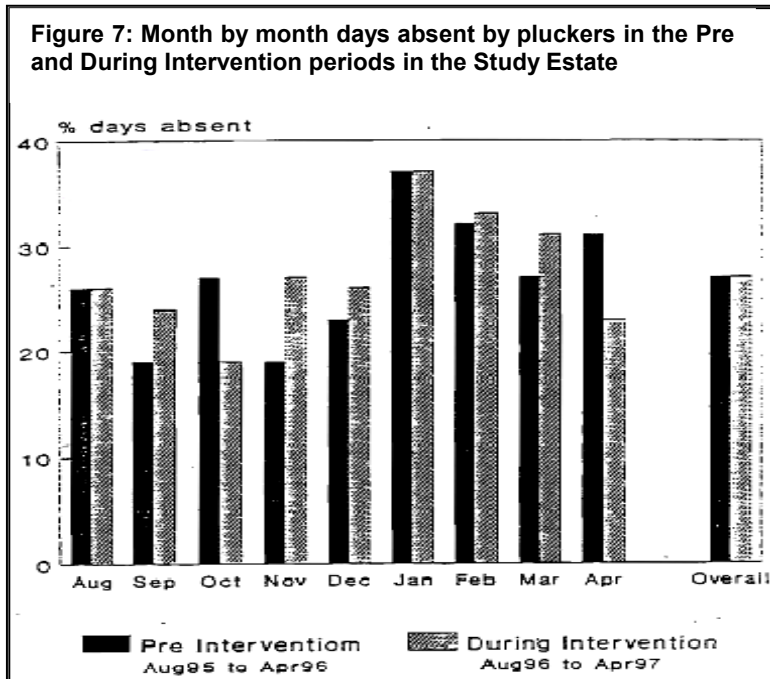
The average tea plucked per worker/per day in the Study Estate from August 1997 to April 1998 was 28 Kgs. It was 26 Kgs during our intervention period of August 1996 to April 1997. It was 23 Kgs for the pre-intervention period of August 1995 to April 1996. The plantation has confirmed that they continued to give the iron supplementation, iodized salt and Vitamin A. They also gave deworming tablets twice a year. The crop yield was also much higher in this period at about 2000 Kgs per hectare was compared to about 1600 Kgs per hectare in the pre- and during-intervention periods. The Management maintains that the better crop is the prime reason for better yield (average tea plucked). However, they concede that the pluckers appear to be 'more healthy and energetic'. In the Control Plantation the corresponding figures were 21 Kgs, 21 Kgs, and 24 Kgs. The average crop yield in 1997-98 was also much better at 2040 Kgs per hectare.

### **Programme implications and recommendations**

The recommendations are as follows:

- Encourage partnerships between the Management of plantations, academia/researchers, and the pharmaceutical/food processing industry to design and deliver simple, cost-effective and sustainable micronutrient interventions of iron, iodine and Vitamin A for the workforce on plantations.
- Build confidence and capacity among the Management/staff of plantations to manage micronutrient interventions on their own.
- Demonstrate how combined micronutrient interventions can be easily integrated into the ongoing health programmes or activities on the plantation.
- Encourage and enthuse the Management, medical and health staff to strongly support preventive health programmes.
- Encourage plantation ration shops to procure and store only reputed brands of iodized salt and to sell it at subsidized rates. Fortification of common foods is the cheapest and simplest way of ensuring that the three micronutrients, namely, iron, iodine and Vitamin A are consumed by the entire workforce and their families. In future, the plantation Managements should seriously think of
- Procuring double fortified salt (iron + iodine) and selling it to the workforce at subsidized rates. Cooking oil likewise can be fortified with Vitamins A, D and E.

- Convince Apex bodies such as the United Planters of South India to make it mandatory to incorporate micronutrient Interventions into the Comprehensive Labour Welfare Schemes (CLAWS)



- Convince the managers that the improvement of the health and well being of their workforce through micronutrient interventions will result not only in better worker productivity but also in more cordial relations between the Management and the workforce.
- Spearhead a movement in the plantation industry

to replicate the Study Estate's success story.

- In the spirit of "each one teach one", we request the Study Estate to become the preceptor and demonstrator of the above Micronutrient Intervention to not just one, but all the plantations in Chikmagalur District.

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## **THE LANCET SERIES ON MATERNAL AND CHILD NUTRITION AND INDIA'S SOLUTION EXCHANGE FOOD AND NUTRITION SECURITY COMMUNITY: HOW DO THEIR CONCERNS AND PRIORITIES COMPARE?**

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In January 2008 the *Lancet* published a five-paper series on maternal and child nutrition that was designed to call global attention to the importance of nutrition as the critical underpinning of health and economic development<sup>1</sup>. Funded primarily by the Bill & Melinda Gates Foundation with additional support from other donors for some of the background papers, the series is aimed partly at the nutrition community but more importantly at the broader public, with the objective of increasing the priority given to maternal and child nutrition in the development agenda. The Series is an important reference point and, while nutrition practitioners will undoubtedly have disagreements with the details<sup>2</sup>, it is a welcome and significant contribution that hopefully will have a major impact on funding, programmes and policy decisions. It is also provocative and aims to stir things up so that significantly more attention is paid to this very serious global problem. As Julian Schweiter, Director, Health, Nutrition and Population Department of the World Bank put it when discussing the importance of the Series: "The messages we need to get out there are that malnutrition kills, it is irreversible, and it creates a next generation of poor, uneducated, unproductive people, more susceptible to early onset of adult chronic diseases<sup>2</sup>."

All of the issues in the *Lancet* series are familiar to the Indian food and nutrition profession. Indeed, a significant portion of the background material and historical analysis cited comes from India. In light of this *festschrift* in honour of Dr. Gopalan and his long and outstanding career, it is important to recognise how well the issues raised by the *Lancet* series are mirrored in his influential output and that of the Nutrition Foundation of India, which he founded. These contributions have kept nutrition in focus as an important factor in Indian national development. Among other crucial topics, this work has highlighted the importance of adolescent girls in the nutrition equation, provided insight and practical training material on how to address nutrition needs in rural areas, showed the way forward in addressing deficiencies of vitamin A and other micronutrients through food-based strategies, and given a clarion call on the need to focus on pregnant and nursing mothers among many other contributions. Dr. Gopalan's leadership and the support of NFI have been of great importance both to the understanding and to the practice of improving the nutrition situation in India, which remains a critical national problem and an "under-prioritised" challenge.

The Food and Nutrition Security Community in India is by now a mature and varied group of practitioners and researchers, working at all levels of activity. How do the themes and recommendations of the *Lancet* Series compare with what is most on the minds of this group? It is difficult, of course, to provide a precise answer to this question, given the geographic and intellectual spread

of the community working on nutrition issues. An interesting insight, however, comes from a review of the interactions of the Food and Nutrition Security (FNS) Community of the knowledge management initiative *Solution Exchange*, of which NFI is a co-convenor along with FAO. The FNS community began in July 2005 and has by now gone through 108 queries and “consolidated replies” that reflect the concerns, experience and opinions of the 1,800 members<sup>3</sup>.

An important characteristic of this *Solution Exchange* community has been the desire to keep agricultural, food security and nutrition interests together, in order to stimulate greater awareness of the issues and experiences by all members and stimulate cross-fertilisation of ideas. Of these 108 queries, around 35 have been focused on nutrition issues, depending on where one draws the line on topics that frequently cover intersecting areas of food and nutrition security. These 35 discussion topics do not, of course, represent a scientific survey of what issues the Indian FNS community sees as most important, but they do provide an interesting window into what the community sees as the burning issues. How do these concerns match the conclusions and recommendations of the *Lancet* Series? What are the gaps or disagreements?

Before turning to a brief analysis of the *Solution Exchange* topics, it is necessary to summarise some of the main points of the five *Lancet* papers which in turn are summaries of a very large body of evidence and literature. The first two papers (“Global and regional exposures and health consequences” and “Consequences for adult health and human capital”) quantify the prevalence of maternal and child undernutrition and the resulting impact in terms of death and disease and long-term education and economic effects. In addition to quantifying the impact of undernutrition, these two papers also introduce the following “key messages”:

- Vitamin A and zinc deficiencies account for the largest remaining disease burden among the micronutrients considered;
- Iodine and iron deficiencies call for sustained effort in order to reduce the burden of disease associated with them;
- Suboptimum breastfeeding, especially non-exclusive breastfeeding in the first six months of an infant’s life, results in 1.4 million child deaths annually and accounts for 10 percent of the disease burden in children under five;
- Maternal short stature and iron deficiency anaemia increase the risk of death during delivery, accounting for at least 20 percent of maternal mortality;
- Poor foetal growth and stunting in the first two years of life lead to irreversible damage;
- Children who are undernourished in the first two years of life and who then rapidly put on weight later in childhood and adolescence are at high risk of nutrition-related chronic disease;
- The prevention of maternal and child undernutrition is a long-term investment that will benefit the present generation and their children.

The third paper (“What works? Interventions for maternal and child undernutrition and survival”) examines the potential benefits from implementing 45 different nutrition interventions, which current evidence indicates would be effective and applicable in low- and middle-income countries. The key messages in this paper are:

- Effective interventions are available to reduce stunting, micronutrient deficiencies and child deaths;
- Counselling about breastfeeding and fortification or supplementation with vitamin A and zinc have the greatest potential to reduce child morbidity and mortality;
- Improvement of complementary feeding in both food-secure and food-insecure populations could substantially reduce stunting and related diseases;
- Interventions in maternal nutrition can improve outcomes for maternal health and for births, but few such interventions have been assessed on a sufficiently large scale;
- Long-term investments are also required to improve the educational and economic status of women and empower them.

The final two papers look at the current state of such interventions and what needs to be done at the national level (paper 4) and the international level (paper 5). At the national level, the key messages are as follows:

- Nutrition should be a priority at national and subnational levels because it is central for human, social, and economic development;
- The period from pregnancy to 24 months is the crucial window of opportunity for reducing undernutrition and this is the period on which programmes and monitoring and assessment should focus;
- There is significant experience and expertise in individual countries on how to meet the challenges, and this is a resource that needs to be shared and used for setting priorities and for problem-solving research;
- Nutrition resources should not be used to support actions that are unlikely to be effective in the context of country or local realities.

At the national level, paper 4 outlines seven key challenges. These are:

- *Getting nutrition on the national agenda:* Nutrition is not the only priority, even for policies and programmes that target women and children, and nutrition programmes compete for resources with other causes. Building political awareness and commitment is vital.
- *Doing the right things:* It is critical to strengthen implementation of interventions that have been shown to be effective.
- *Not doing the wrong things:* It is important to review programmes and policies to ensure that resources are prioritised for those interventions that are likely to improve the nutritional status of mothers and children under 24 months of age.
- *Acting at scale:* Phase in more rapidly and on a wider scale what works, but with an eye on sustainability and local context.

- *Reaching those in need.* Appropriately target those whose need is most critical.
- *Data for nutrition decision-making.* Access better data for decision making, planning and monitoring effectiveness.
- *Building strategic and operational capacity.* There should be a long-term commitment to improving operational capacity including training and evaluation at all levels. This is a key challenge.

Do these themes match the concerns of the nutrition community in India as evidenced by the discussions in *Solution Exchange*? The short answer is yes, and very much so, although there are areas of divergence. To begin with, the objective of *Solution Exchange* is precisely to share experiences on what works and what doesn't in order to reach scale and have national-level impact. The key messages highlighted above from the first three papers in the Series are very similar indeed to the nutrition topics covered in the *Solution Exchange* queries. Furthermore, members of the larger food and nutrition security community also recognise quite clearly that it is necessary to address larger questions of women's empowerment and land rights, improved agricultural productivity and incomes, and other issues that have direct bearing on all areas relating to enhanced livelihoods and well-being. There is also considerable consistency in the specific topics covered.

In the context of the seven themes outlined in paper 4 of the Series mentioned above, it would appear that the concerns of the group could be listed in the following order:

- reaching those in need,
- doing the right things well,
- acting at scale,
- building strategic and operational capacity, and
- accessing adequate data for decision making.

There is no doubt an implicit understanding of the need for political support in getting (or keeping) nutrition on the national agenda but, as ICDS and MDM programmes are already immense by any standard, this may lead to less emphasis within the community on building political awareness and commitment for nutrition. All of the *Solution Exchange* discussions on awareness and communication strategies for example, target the undernourished and not the general public or policy makers.

Breaking these themes down, the largest group of *Solution Exchange* queries, 8 out of the 35, dealt with some aspect of appropriate targeting and reaching those most in need. These queries dealt with tribals, slum dwellers, fisher folk, people living with HIV, adolescent girls and those depending on common property resources, and also with issues such as screening and targeting of preschool children and using panchayats to reach vulnerable groups.

Doing the right things and building on pilot experience to achieve national-level impact were underlying themes in many of the discussions. Interventions for anaemia were discussed in seven queries, and included topics dealing

with double-fortified salt, iron fortification of millet flours, the control of anaemia in pregnancy, reaching out to school adolescents for anaemia control, anaemia in fisher folk, and methods for calculating the incidence of anaemia in school children. Six queries dealt with food-specific or dietary topics: dietary guidelines, nutrient content of green leafy vegetables, trans fat consumption, phytate content in plant foods, blending of edible oils, and increasing the consumption of micronutrient-dense foods. Iodine deficiency disorders and iodised salt were discussed in three queries and one dealt with improving coverage of Vitamin A supplementation. Four queries dealt with aspects of the ICDS or mid-day meal programmes: promoting consumption of vegetables and fruits, decentralised supplementary nutrition, identifying best practices and school feeding programmes and local agricultural development. Finally, one of the queries dealt with overnutrition among rural and urban children.

Strategic and operational capacity was likewise a common theme. Specifically, a strategic focus on improving Infant and Young Child Feeding (IYCF) practices came up in four queries: strategizing goals, communication strategies, community-based approaches and promotion of complementary feeding practices. Data for decision making came up in at least three of the queries: calculating the incidence of anaemia (mentioned above), indices for measuring nutritional status in children and the availability of a common research data base on nutrition and health status (of adults).

What are the areas of divergence? A few specific interventions highlighted in the Series have not yet come up. These include zinc and maternal calcium supplementation, for example. Also, many of the individual comments sent in by members in the context of individual queries do not conform to the specific recommendations of the *Lancet* Series. Several interventions pertain more to the interests of the Child and Maternal Health Community of *Solution Exchange*, which often has a “cross posting” with the FNS Community, and so would not be expected to appear in the FNS community (e.g., zinc management of diarrhoea, hand washing or hygiene interventions and treatment of severe acute malnutrition). More important, however, is a much lower emphasis within the FNS Community on the age group of -9 to 24 months group, contrary to the strong emphasis on this group in the Series. There does not, in fact, appear to be a prioritisation of this group within the *Solution Exchange* queries. Of the 35 queries, only 5 explicitly related to this category (although a number of the queries were not specifically limited to older age groups).

The largest point of contention, perhaps, is the lack of any discussion on “not doing the wrong things”, which for the *Lancet* series authors quite clearly include large Indian programmes that received considerable discussion in the FNS community. In the “challenges” section of the fourth paper on “Effective Action at the National Level,” under *Challenge 3: Not doing the wrong things*, the authors highlight three strategies that “the Series reviews found to be ineffective as direct contributors to reducing undernutrition in mothers or young children: growth monitoring (unless linked to adequate nutrition counselling and referrals); preschool feeding programmes targeting children



over 24 months of age; and school feeding programmes targeting children over 5 years of age.”<sup>1</sup> The paper goes on to say that

“Some of these actions, such as school feeding programmes, could have important, albeit non-nutritional, benefits for education, and countries might decide to continue these programmes with support from the education sector. However, school feeding programmes are targeted to children after the age at which stunting generally occurs and can be prevented, and in fact might have adverse effects if they result in excess calorie intake in children in this age-group.”<sup>1</sup>

In essence, referring to ICDS and mid-day meal programmes, as “the wrong things” is of course highly provocative and contentious. It is natural that much of the discussion within the Indian FNS community has focused on improving the impact of these large national programmes. The Series goes on to say that “The bottom line is that judgments about “right and wrong” (or “effective and ineffective”) are contextual. An important priority is to strengthen research, operational capacities, and institutional mechanisms for making these judgments, assessing the results and sharing experiences”<sup>1</sup>. Nevertheless, the intention of the Series is precisely to call attention to the serious global (and Indian) predicament of child malnutrition, with its enormous consequences for development, and the fact that it is not improving at anywhere near the rate that it could and should be improving. A key recommendation of the *Lancet* Series is, then, to make sure that most resources are directed toward interventions that evidence shows would have the greatest impact.

In conclusion, the *Lancet* Series mirrors the concerns and experience of the Indian food and nutrition security community, as evidenced by *Solution Exchange* interactions. Less consistent is the prioritisation of actions to increase political commitment, and in particular for prioritising nutrition interventions for the -9 to 24 months of age group. There is plentiful material here for further debate and operational refinement and, following the exemplary leadership of Dr. Gopalan; the Indian nutrition community will certainly be well represented in the action on all fronts. It will be both interesting and important to see how the food and nutrition security community in India responds.

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# IMPROVING THE MICRONUTRIENT CONTENT OF FOOD CROPS THROUGH BIOFORTIFICATION

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## Introduction

Access to a healthy diet is a fundamental right of every human being on this planet. Yet a billion people, mostly in developing countries, go to bed hungry every day. Micronutrient deficiencies affect 3 billion people. Malnutrition hinders the attainment of human potential and the nation's social and economic development. Access to food depends on income. Currently, more than 1.3 billion of the world population is absolutely poor, somehow surviving on a per capita income of less than one U.S. dollar/day. Another two billion are marginally better off<sup>1</sup>. Thus, investments in employment generation are as important as investments in food production. The malnutrition problem is further exaggerated by the burgeoning world population, which is likely to reach 8 billion by the year 2030. Most of this increase (93%) will take place in the developing world, whose share of the global population is projected to increase from 78% in 1995 to 83% in 2020.

In addition to protein-energy malnutrition, deficiencies of minerals and vitamins affect a high proportion of the world's population, particularly in the developing world. Thus, organizations such as the World Health Organization<sup>2</sup>, and more recently the Consultative Group on International Agricultural Research<sup>3</sup>, have accorded high priority to fighting this 'hidden hunger' (i.e. micronutrient deficiencies). Deficiencies in the micronutrients iron (Fe), zinc (Zn), iodine (I) and vitamin A have been targeted for intervention, given the immense magnitude of the problem posed by these deficiencies amongst the world's poor. Estimates are that two billion people world-wide are Fe deficient, with consequent diminished work performance, impaired body temperature regulation, impaired psychomotor development and intellectual performance, altered behavioral changes (e.g. significantly decreased responsiveness and activity, and increased body tension and fearfulness), decreased resistance to infection and increased susceptibility to Pb poisoning<sup>4</sup>. Women and children are particularly at risk of Fe deficiency because of their higher requirements for childbearing and growth, respectively. An estimated 58% of the pregnant women in developing countries are anaemic, and their infants are more likely to be born with a low birth weight. WHO estimates that 31% of children under 5 years of age in these countries are also anaemic. At least 400 million people worldwide have vitamin A deficiency, and more than 100 million of those are young children. Annually, three million children die as a result of vitamin A deficiency. Fourteen million children suffer from clinical eye problems, and increased risk of respiratory diseases and diarrhoea<sup>5</sup>.

One billion people reside in I-deficient regions, with numerous inhabitants of these areas suffering from I-deficiency disorders, including goitre, cretinism, lower intelligence quotients and increased prenatal mortality<sup>6</sup>. Zn deficiency, thought to be widespread, can lead to retarded growth, depressed immune

function, anorexia, dermatitis, skeletal abnormalities, diarrhoea, alopecia, increase in medical complications, and mortality during childhood, if such a deficiency persists for a prolonged duration<sup>7</sup>. Furthermore, Zn deficiency in humans has been linked to vitamin A underutilization<sup>8</sup>. Even in the developed countries, micronutrient deficiencies affect significant numbers of persons in the population. Taken together, micronutrient deficiencies affect a far greater number of people worldwide than protein-energy malnutrition does.

### **Tackling micronutrient malnutrition**

Intervention programmes, including supplementation, food fortification and nutrition education, have been successful in reducing malnutrition in specific situations, and will need to be continued in the future. For example, the salt fortification with iodine has been shown to be effective in many countries. The programme is inexpensive and reach many of the sections of the population who are most at risk<sup>6</sup>. However, for the micronutrients Fe, Zn and vitamin A such programmes are expensive, with recurring annual expenditures, and are unlikely to reach all those at risk. Moreover, these intervention programmes have often been suspended for economic, political and logistical reasons.

Nutritionists agree that part of the solution to micronutrient deficiencies is to convince the population to make their diets more nutritious. So far, however, attempts to change eating behavior have been unsuccessful. It is often difficult to make dietary changes using local foods if you are poor. One project designed to increase vitamin A consumption among the poor in Northeast Thailand showed positive results. The project promoted vitamin-rich foods as those used by loving and caring mothers, focusing on a locally grown vegetable, ivy gourd (*Coccinia grandis*), which is rich in vitamin A and which they themselves could cultivate. Most projects that seek to change diets, however, end with participants returning to their old ways. Such approaches have worked only in limited settings. They require a lot of inputs, constant follow-up and education. When they are scaled up, they rarely work, so they tend not to be sustainable. Under these limitations, breeding for trace-mineral-dense seeds has been considered most effective for tackling micronutrient deficiencies<sup>9, 10</sup>. Crop varieties with mineral-dense seeds are not only useful in the alleviation of hidden hunger, but also suitable for growing on trace-mineral-deficient soils. Results from Australia and elsewhere show that, where the soil is deficient in a particular micronutrient, seeds containing more of that nutrient germinate more efficiently, and have better vigour and more resistance to infection during the vulnerable seedling stage. These benefits can, in turn, result in higher grain yields. Thus, priorities for human and plant nutrition may often coincide.

The new strategy for supplying micronutrients to the poor in developing countries involves making the staple foods they eat more nutritious through the use of conventional plant breeding and biotechnology. This strategy is low-cost and sustainable, does not require a change in eating habits, and does not impose the recurring costs that accompany fortification and supplementation. The greatest potential for improving the nutritional status of populations on a large scale involves breeding micronutrient-dense staple

crops (biofortification), which can feed world's poor. Biofortification efforts are underway in the case of several food crops.

### Improving the amount and bioavailability of Iron and Zinc

A research project to develop improved rice varieties with high Fe and Zn contents was initiated at the International Rice Research Institute in 1992, with screening of germplasm to identify donors. About 7000 entries have been analyzed in collaboration with the Department of Plant Science, University of Adelaide, Adelaide, Australia a lot of variation was observed in the rice germplasm with regard to both Fe and Zn contents in the grain. Among a subset of 1138 samples analyzed, Fe concentrations ranged from 6.3 to 24.4 mg/kg, with a mean value of 12.2 mg/kg. For Zn, the range was 15.3-58.4 mg/kg. A comparison of the Fe and Zn contents of selected varieties with those of widely grown varieties IR 36 and IR 64 is shown in Table 1.

Variety	Fe (mg/kg)		Zn (mg/kg)	
	Mean	SE	Mean	SE
Zalmagna	22.0	1.4	31.8	7.7
Zuchen	20.2	1.8	34.2	5.0
Xua Bue Nuo	18.8	0.8	24.3	0.7
Madhukar	14.4	0.5	34.7	2.8
IR64	11.8	0.5	23.2	1.4
IR36	11.8	0.9	20.9	1.4

Traditional varieties Jalmagna and Zuchen contained almost twice as much Fe and 50% more Zn when compared with IR36 and IR64. A number of aromatic rice varieties such as Basmati 370 from India and Pakistan, and Azucena from the Philippines also showed consistently higher Fe and Zn contents<sup>11</sup>. Ortiz-Monasterio and Graham<sup>12</sup> found a four- or five-fold variation between

the lowest and the highest Fe and Zn concentrations in grains among several hundred wheat accessions. The highest concentrations in some cultivars were twice those of the popular modern cultivars.

Rice plant varieties with high Fe and Zn contents are tall, traditional, and low yielding, and hence not suitable for modern agriculture. Efforts are underway to develop improved breeding lines with elevated levels of Fe and Zn. Crosses between these traditional varieties and high-yielding varieties have produced progenies with both high yield and high levels of these micronutrients. For example, an improved breeding line with short stature, IR68144-3B-2-2-3, from crossing a high-yielding variety IR72 with the tall traditional variety Zawa Bonday from India, has a high concentration of Fe, approximately 21mg/kg, in brown (i.e. unmilled) rice. Its yield potential is comparable with that of improved rice varieties. A human efficacy study using milled rice of this variety carried out during a 9-month feeding trial among young Filipino women<sup>13</sup> showed that a 17% higher total dietary iron consumption from biofortified rice resulted in a modest increase in serum ferritin and total body iron. Interestingly the response was greater in non-anaemic subjects for ferritin and body iron. This study proved that the consumption of biofortified high-iron rice increased the body iron by 20%.

It also appears possible to raise the micronutrient content of cereals through genetic engineering. For example, Goto *et al.*<sup>14</sup> transferred the soybean

*ferritin* gene into the rice variety Kitaake through *Agrobacterium*-mediated transformation. The promoter for the rice-seed storage protein glutelin GluB-1 was used to localize the expression of the soybean gene specifically in the endosperm. The Fe content of the transgenic seeds was as much as threefold greater than that of untransformed controls. Similarly Lucca et al.<sup>15</sup> introduced the *ferritin* gene from the common bean into rice, and these transgenic rice lines had double the amount of Fe in seeds as compared to the controls.

Another genetic engineering approach for increasing the bioavailability of Fe in rice diets is the elimination of phytate. This sugar-like molecule binds a high proportion of dietary Fe, so that the human body is unable to absorb the Fe. Lucca et al.<sup>15</sup> introduced a fungal gene for the enzyme phytase. This breaks down phytate, thus improving the bioavailability of Fe in rice diets. Rasmussen and Hatzack<sup>16</sup> isolated Na<sub>2</sub>O-induced mutants of barley with low phytate contents. The levels of free phosphate were higher in these mutants. The results indicate the possibility of improving the nutritional value of crops through mutation breeding. Studies at CIAT (International Institute of Tropical Agriculture) showed that certain varieties of the common bean had as much as 60-80% more Zn than those of commercially grown varieties. Breeding efforts are underway to incorporate higher levels of Zn into improved varieties<sup>17</sup>

### **Improving the Vitamin A content**

As mentioned above, poor people whose diets consist primarily of cereal grains and tubers show a prevalence of serious vitamin A deficiency. Therefore, the focus of crop improvement for enhancing vitamin A is on cereals and tuber crops.

#### **Rice**

Rice grains do not contain  $\beta$ -carotene, the precursor to vitamin A. However, they do contain geranylgeranyl pyrophosphate, which can be converted to  $\beta$ -carotene by a sequence of three enzymes in the vitamin A biosynthetic pathway. The three genes for these enzymes, two (*psy* and *lyc*) from daffodil (*Narcissus pseudonarcissus*) and one (*crt1*) from the bacterium *Erwinia uredovora*, were introduced into the rice variety Taipei 309 through *Agrobacterium tumefaciens*-mediated transformation. One to three transgene copies were found in transformed plants. Ten plants harbouring all three introduced genes showed the normal vegetative phenotype, were fully fertile, and had yellow endosperms, indicating carotenoid formation. Extracts from the coloured grains were analyzed, and the goal of providing at least 2 $\mu$ g provitamin A/gm seems to be realistic<sup>18</sup>. The rice variety Taipei 309 was used for introducing the  $\beta$ -carotene biosynthetic pathway, as it is easy to transform. Further research has shown that the presence of only two genes, *Psy* and *crt1*, are sufficient to establish the biosynthetic pathway leading to development of  $\beta$ -carotene in rice endosperm. When *Psy* from maize and *crt1* were introduced in the US rice variety Cocodrie, the  $\beta$ -carotene level was 23 times of that of transformed Taipei 309. Taipei 309 is not cultivated while Cocodrie is not suitable for growing in Asia. Moreover, information on

bioavailability and food safety of the so-called “golden rice” is necessary before it can be commercialized. To oversee further development of golden rice, Golden Rice Humanitarian Board (HumBo) ([www.goldenrice.org](http://www.goldenrice.org)) was established. Under the auspices of the HumBo, programmes to transfer *psy* and *crt1* genes from transformed *Cocodrie* into varieties commercially grown in Asia through backcrossing are underway. Six countries (India, Indonesia, Myanmar, Bangladesh, Philippines and China) have undertaken such projects. The backcrossing programme is most advanced at IRRI where popular Asian rice varieties IR 36 and IR 64 are being used as recurrent parents<sup>19</sup>. At present BC2 F3 progenies are being evaluated in contained field trials. Bioavailability and food safety evaluations are under way. It is expected that golden rice will be available for commercial production in 2011.

### Cassava

Root Color	Numerical Scale	Carotene Mg/100gm	Standard Deviation
White	1	0.13	0.48
Cream	2	0.39	0.28
Yellow	3	0.58	0.28
Deep Yellow	4	0.85	0.17
Orange	5	1.26	0.11

Cassava is an important staple for 50 million poor people, particularly in Africa where vitamin A deficiency is rampant. Genetic variation in respect of  $\beta$ -carotene in cassava roots is high. Orange-coloured roots have 9 -10 times more  $\beta$ -carotene

than white roots do (Table 2). The Harvest Plus Program<sup>20</sup> (Breeding Crops for Better Nutrition) of CGIAR is identifying orange-coloured clones with superior agronomic traits with a view to popularize them.

### Sweet Potato

Orange-fleshed varieties of sweet potato are rich in vitamin A. However, consumers in Africa and elsewhere prefer white-fleshed varieties, which are devoid of vitamin A. An action project was implemented by the Kenya Agricultural Research Institute (KARI), Nairobi, Kenya, in collaboration with the International Potato Center (CIP), Lima, Peru. Orange-fleshed varieties, both high yielding and rich in  $\beta$ -carotene were introduced to women farmers. The result was that orange-fleshed sweet potatoes, whether eaten alone or as ingredients in processed foods, were highly acceptable to both processors and consumers. Using standard methods of analysis it was demonstrated that the increased consumption of these sweet potatoes did indeed contribute to the alleviation of vitamin A deficiency in case study households<sup>21</sup> (Hageniwana 2000). In the eastern and southern areas of Africa, sweet potatoes are an important source of calories for poor people. Most of the sweet potato varieties grown there are white-fleshed and thus lack  $\beta$ -carotene. Under a special project “Reaching end-users of orange-fleshed sweet potato in east and southern Africa” the Harvest Plus programme<sup>20</sup> (Harvest Plus, 2006) is popularizing orange-fleshed sweet potato varieties amongst poor populations of crop growers and consumers.

## **Maize**

Maize is a dominant subsistence crop in much of sub-Saharan Africa and the Americas, where 17 to 30 % of children under the age of 5 years are deficient in vitamin A. Most of the maize consumers in Africa prefer white maize, which is devoid of  $\beta$ -carotene. A team consisting of scientists from Cornell University, the University of Illinois, Boyce Thompson Institute, DuPont Crop Genetics and International Maize and Wheat Improvement Center (CIMMYT) is working on improving the  $\beta$ -carotene content of maize. The project analyzed 300 genetic lines of maize selected to represent the global diversity of maize, and identified some varieties that came close to the target amount of 15 micrograms of  $\beta$ -carotene per gram as compared to as low as 0.1 microgram per gram in standard varieties<sup>22</sup> (<http://www.news.uiuc.edu/news/08/0117maize.html>).

## **Wheat**

Strong carotenoid pigmentation was present in older bread-wheat varieties. However, during this century market demand has driven wheat breeding to be focused on the production of wheat for white flour. The earlier varieties could be brought back into breeding programmes if desired.

## **Bananas**

The Queensland University of Technology, Australia, has developed transgenic bananas containing  $\beta$ -carotene, vitamin E, and Fe. The introduction of the *psyB73* gene from maize and *crt1* from *Erwinia uredovora* led to the establishment of the biosynthetic pathway for the production of  $\beta$ -carotene. Genes for enhanced iron content and vitamin E have also been incorporated. The university has applied for a license to the Australian Government for international release of these the biofortified bananas<sup>23</sup> (<http://www.oqtr.gov.au>).

## **Improving the amino acid balance**

Human diets derived from cereal grains are deficient in some of the ten indispensable amino acids that are required for normal growth and development. Lysine is the most limiting amino acid. A natural variation in maize germplasm was exploited to develop quality protein maize (QPM) at CIMMYT in Mexico. The *opaque2* gene was incorporated into maize varieties through breeding, and it led to the doubling of lysine and tryptophane. QPM maize varieties have been released in several countries in Africa and are grown on almost a million hectares<sup>24</sup> (Pray *et al.*2007). Millions of people in sub-Saharan Africa suffer from health problems associated with vitamin and mineral deficiencies. The Africa Biofortified Sorghum (ABS) project seeks to find a long-term solution using biotechnology to create “super sorghum” that grows well in harsh environments and also contains high levels of essential nutrients. The project, funded by the Bill and Malinda Gates Foundation under its Grand Challenge for Health programme, aims to develop more nutritious and easily digestible sorghum containing increased levels of essential amino



acids, especially lysine and vitamin A and E, and more Fe and Zn. The Africa-based food organization, Africa Harvest, is partnering with scientific teams from DuPont through its subsidiary Pioneer Hi-Bred International and the Council for Scientific and Industrial Research in South Africa to make this project a reality<sup>25</sup> (<http://www.supersorghum.org>).

Biotechnology approaches are being used to enhance the lysine content of rapeseed, corn and soybean. The introduction of bacterial genes for dihydrodipicolinic acid (DHPHS) and aspartokinase(AK) enzymes encoded by the *dapA* gene from *Corynebacterium*, and the *lysC* gene from *Escherichia coli* led to a five-fold increase in lysine in canola, corn and soybean<sup>26</sup>. Similarly, the amino acid profile and total protein content of potato was improved through introduction of the *AMA11* gene from *Amranthus hypochondriacus*<sup>27</sup>. The biofortified potatoes have been evaluated in field trials and now await a decision from the regulators with respect to approval or need for further testing<sup>28</sup>.

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# BIOACTIVE SUBSTANCES AND FUNCTIONAL FOODS

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## Introduction

Throughout the world, including Asia, consumers are looking for health foods that can not only prevent diseases but can promote health and well-being. New science-based investigations are emerging, which appear to confirm the wisdom inherent in the traditional use of some of these foods, and to support the long history of the use of such foods by humans. Mounting health care costs and the consumer's desire to maintain health and quality of life, have focused the attention of biomedical researchers and public health scientists on diets and disease prevention.

Alternative therapy or complementary therapy with plant-based medicinal foods is rapidly gaining attention, both within the scientific community and among consumers. Foods sculpt the body's needs for nutrients and phytonutrients. They have several physiological and biochemical advantages, and are nowadays particularly being considered for their beneficial effects in the context of chronic ailments. Most of the bioactive constituents appear to modify the aetiopathological processes of atherosclerosis, inflammation, immunopathology, and carcinogenesis. This article, which is being written in honour of Dr.C. Gopalan on his 90<sup>th</sup> birthday will, I hope, be a fitting tribute to him, as he has been championing food-based approaches to tackle nutritional disorders and has always preferred dietary approaches. He says, "Look towards Farms and not towards Pharmacies for prevention of nutritional diseases and promotion of health". While identifying active compounds in foods is a scientific approach, the complete foods are more relevant to health and disease, given that the food matrix impacts availability, interactions and responses. The origin of all functional foods is based on the science of analytical epidemiology, and it is essential to understand that there may not be uniformity in responses .

Ancient Hindu religious literature (Vedas) says that "Annam is Aham" meaning 'you are what you eat' and Hippocrates declared "Let food be your medicine and medicine be thy food". Current science reinforces these statements and the food markets today, particularly in the Western world, are full of functional/novel foods or nutraceuticals. Technological advances have helped to develop products in concentrated forms, or in forms that can be easily assimilated, or as combinations of foods for greater benefits. It must be stated here that foods are natural sources of nutrients and a diversified diet can be a rich source of all the necessary bioactive substances. It can very effectively impact pathological processes that lead to deficiency and chronic disorders. Nutrition education and food guides can help to promote food-based approaches for all biologically effective molecules. Japan is the first country that explored the boundary between food and medicine. India is a land of herbal products and plant-based vegetarian diets. Countries like China, Korea and Srilanka are also steeped in the medicinal food tradition. Wider acceptance of the medicinal value of foods and their use will cut down the

health care costs as well. However, it is important to provide science-based evidence of their biological functions. The health benefits of functional foods should, in fact, extend beyond their macro- and micronutrient composition<sup>1</sup>. A functional food or a medicinal food is any fresh or processed food claiming to have a health-promoting and/or disease-preventing property beyond the basic nutritional function of supplying nutrients, although there is no consensus on the exact definition of these terms.

However, it is important to realise that it is not always possible to ascribe therapeutic benefits to individual components; even if such components are identified it may not be possible to get the maximum benefits of isolated compounds unless they are given as part of a food-based approach. In other words, the reductionists approach may not be meaningful; it is the holistic approach that can work. In foods, the bioactive constituents may have synergistic or additive effects. Multiple food components may result in the desired effects, from a particular food matrix. More information on molecular and cellular effects of bioactives will be critical in the development of effective and or proactive approaches to reducing the burden of diseases. Strategies for identifying those who will benefit most from dietary intervention are also needed if public health messages are to be effective and have meaningful impacts on health and well-being. Current literature accords great importance to the long history of human use of a variety of foods, as they are likely to yield novel drug prototypes for chronic diseases such as cardiovascular (heart attack), cerebrovascular (stroke), and neurodegenerative (Alzheimer's and multiple sclerosis) conditions, as well as in cancer, inflammatory problems such as arthritis, cataract, and toxicity caused by drugs and toxins.

### Biological effects

Table 1: Benefits of functional components
➤ general tonic / energy giving / health promoting food
➤ hypolipidemic food/ hypotensive or cardiovascular protectant
➤ immune potentiator
➤ hormone regulator
➤ gastrointestinal function modifier
➤ modifiers of glycemic response
➤ memory enhancers
➤ bone health modifier
➤ promoters of healthy skin
➤ reducers of risk of cancer
➤ weight reducing agents
➤ ageing modifiers

Foods and food ingredients, singly or in combination, have been investigated for their biological effects that could potentially protect against cardiovascular pathology, cancer risk, inflammation, immune suppression, bone problems, neurological damage, suboptimal performance levels, problems associated with the gastrointestinal tract, and hormone-related problems, besides actively promoting good all-round health

and general well-being (Table 1)<sup>2</sup>. Thus bioactives have a role beyond mere nutrition support. They are substances that are useful in preventing disease and ill-health and also in actively promoting health.

### Bioactive compounds

Many bioactive substances have been identified . As on date, more than 500 compounds have been identified and tested for biological functions and mechanisms of action<sup>3</sup>. Some of these are listed in Table 2. Some families of

<b>Table 2: Bioactive compounds</b>	
<b>Bioactive compounds</b>	<b>Food Source</b>
Simple phenols	Most vegetables/spices/beverages
Carotenoids	Green/yellow/orange vegetables/fruits
Flavonoids	Vegetables/fruits/ tea
Indoles/ Isothiocyanates	Cruciferous/Brassica vegetables
Glucosinolates	Cruciferous vegetables
Organosulfides	Allium vegetables
Polyphenols	Fruits/cruciferous vegetables/nuts/spices
Protease inhibitors	Potatoes/beans/nuts/cereals
Phytoestrogens/isoflavines	Soya/soy products
Epigallocatechin gallate	Green tea
Lycopene	Tomatoes
Limonene	Citrus fruits
Pre&probiotics	Dairy products
<b>Nutrients</b>	<b>Food Source</b>
B.complex vitamins	Green leafy vegetables/nuts/pulses
Vitamins E, C	Citrus fruits/cereals/vegetables
n-3 fatty acids	Fish/oil/green leafy vegetables/spices/nuts
Minerals (Ca,Mg,K,Fe)	Several vegetables/milk & dairy products
Fibres	Vegetables/fruits/cereals/legumes
Low energy foods	Most vegetables/fruits

fruits and vegetables have characteristic components that may confer a particular health benefit. Cruciferous vegetables are sources of glucosinolates and their products, isothiocyanates and indoles. Allium vegetables contain allicin. Allyl sulphides and allicin in garlic give it its distinctive flavour. Green, leafy vegetables are sources of folate, iron, calcium and carotenoids, while tomatoes contain high levels of lycopene. All these components, as well as other phytochemicals, have potential health benefits.

### Mechanisms of action

The bioactives, as present in foods, can be termed as functional foods. When consumed as foods they elicit biological responses. There are several mechanisms by which the bioactives elicit the response. Most of them have strong antioxidant potential while others act by modifying xenobiotic metabolising enzymes, altering lipid metabolism, or altering steroid hormones as shown in Table 3.

The interaction between the diet and phytonutrients is a complex field, as thousands of dietary components are consumed each day (>25000) through routine diets. Dietary bioactives may modify a multitude of processes in normal cells. A single, bioactive food constituent can modify multiple steps in molecular and cellular events such as nutrigenetics, nutritional epigenomics, nutritional transcriptomics, proteomics and metabolomics. Many of these processes can be influenced by several food components. Further, the dose, timing, duration of exposure, and

**Table 3: Mechanisms of action**

- Antioxidant activity
- Modulation of activating and deactivating enzymes.
- Anti-inflammatory response and altering immunity
- Alterations of lipid and lipoprotein metabolism and platelet reactivity
- Stabilising endothelial functions and vascularity
- Altering hormone metabolism
- Antibacterial and antiviral activity
- Cellular division, differentiation, apoptosis and DNA stability and repair.

interactions may alter responses and ultimately the phenotype or manifestations.

Human beings are constantly exposed to genotoxic damage due to activation of foreign compounds, which result in oxidative metabolites. These are further metabolised to watersoluble compounds through the action of deactivating enzymes. This renders them less toxic, and they are eliminated from the body. The biotransformations, pharmacokinetics, pharmacodynamics and toxicokinetics will depend on pharmacogenetic variations of xenobiotic metabolising enzymes that are responsible for inter-individual responses, risk of toxicity, and consequent disease.

Inflammatory reactions are hallmarks of chronic diseases. Several foods can impact inflammatory cytokines, angiogenesis, reactive oxygen and nitrogen species, and eicosanoids. Cellular proliferation, differentiation, and cell death are important events that can respond to various food items. So is the case with DNA stability, damage and repair. Both endogenous substances and exogenous agents (food ingredients) can impact these processes. Thus, a variety of foods, through a variety of mechanisms, either collectively or singly, can exhibit several actions that promote health and well-being and delay the onset of age related malfunctions and pathogenesis of chronic ailments.

### **Development of functional foods**

The development of functional foods requires a multidimensional approach<sup>4</sup>. In order to meet consumer needs under the existing food regulations, nutritionists, food chemists, food technologists, biochemists, toxicologists and clinicians must work together to produce a product or to claim the appropriate health benefits of existing foods. Epidemiological investigation may provide evidence-based scientific information, which needs to be studied experimentally for biological responses, using appropriate biomarkers. Further, these will need to be tested in clinical trials for establishing their health benefits or risk-reducing effects. Foods such as cereals, pulses, nuts, vegetables, fruits, beverages and spices have been widely studied. Genetic manipulations to increase the content of active ingredients may also be useful for enhancing bio-potency (for example, omega 3 eggs, golden rice). Technological innovations can improve the product (for example, soy fermented sauces, pre- and probiotics). It is also possible to add a bioactive to a traditional food (for instance guar gum, fenugreek powder or bran). In such situations, it is necessary to keep in mind the bioavailability of both the active and other physiologically relevant ingredients. The next few sections encapsulate some effects of functional foods which deserve attention, as they are not only commonly used but can be marketed as functional foods for their potent biological effects.

### **Dietary fibres**

Dietary fibres are cardio-protective, as they decrease cholesterol and triglyceride levels, thereby reducing the risk factors for cardiovascular disorders<sup>5</sup>. The concept of fibre and its physiology has advanced

considerably, even though it is still not defined properly. It does encompass a broader range of ingredients than was originally described. Nondigestibility and nonabsorbability in the small intestine are the *sine qua non* characteristic of dietary fibre. It currently includes resistant starch as well as oligosaccharides. Synthetic food fibres have similar properties. As these fibres pass through the gut, they are fermented by the microflora. This process is of physiological importance. Fibres reduce the toxic components in faeces and have prebiotic effects (fructans). Their functions include stool bulking, laxation, fermentation and gut health, hypocholesteremic and triglyceridemic actions, as well as postprandial reduction of glucose and insulin levels. The terms “soluble” and “insoluble” are no longer being used. This is because some insoluble fibres are fermented while not all the soluble fibres affect fat and glucose absorption. They are primarily carbohydrate polymers that are components of plant cell walls, and include cellulose, hemicelluloses, glucans, pectins, gums, mucilages, oligosaccharides and inulin, resistant starch, fructo- and galacto-oligosaccharides, modified celluloses, and lignins. The major sources of food fibre are cereal grains, pulses and legumes, vegetables and fruits. In large epidemiological studies in men in the highest quintile of fibre intake (~ 30g) the death rate due to coronary disease was reduced by 30-40%. Therefore fibre, either in its naturally occurring form in foods or added as a dietary supplement, is encouraged as a method of lowering the incidence of CVDs.

### **Fenugreek seeds**

Fenugreek (FG) or *trigonella fenum graecum*, a spice introduced into India from South-West Asia and South-East Europe, belongs to the family of leguminose. The dried seed is used as a spice while the leaves are used as vegetables. India is one of the major producers and exporters of fenugreek. The estimate of its nutritive value shows it to be a rich source of protein, fibre and omega 3 fatty acids. Several experiments carried out in animals showed that fenugreek incorporated into the diet at 5, 10 and 20% levels produced a hypolipidemic effect<sup>6</sup>. This functionality was attributed to its fibre content galactomannan. The seeds contain 48% by weight of fibre and 2% omega-3-fatty acids. In a randomised, cross-over design metabolic study of NIDDM cases, fenugreek was administered to subjects (100g defatted fenugreek powder) for 10 days<sup>7</sup>. There was a significant reduction in blood glucose leading to an improvement in glucose tolerance. Fenugreek seeds, as such or debitterised, exhibited hypocholesteremic and hypotriglyceridemic effects. In subjects who received FG for a period of 20 days as unleavened bread in a dose of 25g on alternate days, there was a significant reduction in urinary glucose excretion accompanied by reduction in cholesterol and triglycerides<sup>8</sup>. Its hypoglycemic effect has not been fully explained in terms of the fibre present, and therefore IV GTT was performed in type 2 diabetic subjects. The results indicated that, even after intravenous administration of glucose, there is a significant reduction in the AUC and half-life, with a significant increase in the clearance as well as RBC insulin receptors. Obviously there is increased peripheral glucose utilization as well<sup>9</sup>. Further studies were done in experimental animals to study the effects of FG on cataract in chemically induced diabetes. The results showed that 10 and 20% levels of FG in the diet

led to a significant impact. The biochemical parameters of cataractogenesis were altered and, in the obese animals, there was a significant reduction in glucose, cholesterol and triglycerides when compared with the results following administration of 2.5% of galactomannan isolated from fenugreek. These effects were due to increased bile acid excretion. A peculiar amino acid, 4-hydroxyisoleucine, extracted from fenugreek seeds, exhibits insulinotropic activity<sup>10</sup>. Thus fenugreek seeds have great potential as a functional adjunct in the treatment of diabetes. Several recipes have been developed in the Indian context. The gel-forming property of fenugreek fibre reduces gastric emptying, glucose absorption and insulin response. A mild improvement in clinical symptoms such as polydipsia and polyuria was observed in a majority of the patients, with a reduction in anti-diabetic drug doses. Incorporating just around 25 g fenugreek seeds in the daily diet can serve as an effective supportive therapy in the management of diabetes.

### **Omega 3 fatty acids**

Nutritional pharmacology apparently developed as a corollary to medical pharmacology, especially in the management of cardiovascular problems. Based on the epidemiological data in Eskimos, who are fish consumers, it was considered important to study the effects of omega 3 fats. Literature is replete with evidence that omega-3 fats have several biological effects, and the dietary guidelines of all countries suggest the inclusion of fish for the prevention and management of CVD. Omega 3 fats reduce lipids and lipoproteins, blood pressure, cardiac arrhythmias (electrophysiology), vascular reactivity, and endothelial function, and have antiplatelet and anti-inflammatory activity<sup>11</sup>. While DHA affects lipids and lipoproteins, blood glucose, and heart rate, the mixture of EPA and DHA reduces platelet aggregation. Long-chain n-3 fats reduce triglyceride levels significantly<sup>12</sup>. In a long-term intervention study with fish oil (1g/d) for 3.5 years, the group taking fish oil showed 20% reduction in total mortality, 30% decreased mortality on account of cardiovascular events, and 45% decrease in sudden deaths<sup>13</sup>. Thrombotic and arrhythmic events were much fewer in a group that received ALNA, though, in this study, other inputs such as fibre and antioxidants were also altered. Although most studies in secondary prevention support the beneficial effects of omega-3 fats, it is not very clear whether these fats will be of use in primary prevention. The results of several studies have suggested that long-chain omega-3 fatty acid intake is associated with a reduced risk of numerous other diseases such as cancers, immune disorders, asthma, and neurologic disorders. In addition to their benefits in the context of CVD and restenosis, they are thought to be useful for therapy of arthritis, psoriasis, and ulcerative colitis .

### **Other functional foods for CVD prevention**

Since a single ingredient or fish alone may not be the total answer, combinations of functional foods are currently being investigated. A portfolio diet is being recommended, with functional foods such as soy protein(25g), flavonoids, nuts(1.5 ounces almonds), viscous fibre plant sterols (1.3g), and plant stanol esters (4g), all of which reduce LDL by 4-7%<sup>14</sup>. Fibre from



vegetables, fruits, and grains contains soluble fibre. In a clinical trial, this diet was found to be as effective as statins in reducing LDL (30%). It decreased C-reactive protein as well. The Mediterranean diet is a functional diet that is protective against CVD as illustrated by the Lyon Diet heart study<sup>15</sup>. It consists mainly of abundant fruits and vegetables, fish (0.5-1.8g/d of EPA and DHA), nuts, wine and olive oil. There is very little intake of red meat, and the diet in general is low in saturated fats. Similarly, flaxseed, garlic (one fresh clove), black tea, psyllium (1g/d), nuts(phenols, flavonoids, isoflavonoids, phytosterols), cocoa(flavonoids), walnuts (ALNA-1.5 oz/d), red wine (resveratrol8-16oz./d for reducing platelet aggregation) are all functional foods that impact the CVD risk profile<sup>16</sup>. A recent meta-analysis using principal component analysis of several randomised studies dealing with combinations of functional foods and their cardio protective effects, showed significant results. Two principal components were adequate to explain the hypolipidemic results<sup>17</sup>. Phytosterols and fibre had a hypocholesterolemic effect, while n-3 fatty acids lowered triacylglycerol. Thus, mixtures of functional foods or food-based approaches appear to be more attractive than the use of single foods.

### **Anticarcinogens**

Several epidemiological studies reinforce the fact that cancer is a complicated, multifactor, multistage, and multi-manifestation disease with the process of initiation and final manifestation being separated by a long latency period. Hence it is difficult to establish a cause-and-effect relationship between a particular item of the diet and cancer. Several may be interrelated. One study estimated that almost 35% of all cancers may be attributed to dietary factors<sup>18</sup>. Similar estimates have been made by others as well. Therefore dietary and life-style modifications are of prime importance in prevention of cancers, of various types and at various sites. The medical literature provides mechanistic evidence for the role of several of the dietary substances. Molecular mechanisms further reinforce a role for dietary ingredients through gene-nutrient interactions. Dietary antimutagens and anticarcinogens have a role to play by preventing the damage to macromolecules, particularly DNA, through several mechanisms including gene expressions, epigenetic mechanisms and growth inhibition by shutting off proliferative messages, inhibition of cell division, promoting apoptosis, differentiation, telomerase inhibition and angiogenesis inhibition. Research reaching into the fields of genetics, epigenetics, proteomics and metabolomics is required in order to understand the role of diet in the cancer process<sup>19</sup>.

### **Turmeric as a functional cancer-preventing agent**

Turmeric, an Asian spice labelled as a “poor man’s spice” or as “salt of the Orient” is not only known for its colour, aroma and taste, but is being researched all over the world for its preventive and therapeutic benefits. Derived from the rhizome, the root is routinely used as a spice in Indian cuisine. Ayurveda, an ancient system of medicine originating in India, has eulogized spices as wonder foods. In this connection, turmeric and its active principles — curcuminoids — have received considerable attention among biomedical scientists, medical professionals, pharmacologists, food scientists

and nutritionists all over the world. Literature is replete with mounting evidence that agents such as turmeric and its constituents, curcuminoids, promote health and prevent diseases<sup>20</sup>. Turmeric (along with its active principles, curcuminoids) has pleiotropic effects and has received considerable attention as an anti-inflammatory, antiatherosclerotic and anticancer agent<sup>21</sup>. It exhibits several molecular targets and is similar to many other phenolic compounds found in other spices, in fruits and vegetables, and in beverages such as tea and wine(see reference 21 for cross references). Traditionally, turmeric has been used as a food preservative, as it protects and preserves foods against spoilage and infestations. It masks off flavour and protects against decomposition and bacterial spoilage. These traditional practices are now supported by new scientific evidence, and apparently the constituents which protect the plant and food also protect several biomolecules of the body, preventing degenerative disorders that result in chronic diseases. The properties and uses of turmeric/curcuminoids are truly kaleidoscopic.

Traditionally, turmeric has been used as a general tonic, as an anti-infective, and also for skin ailments, wound healing, gastrointestinal and respiratory disorders, arthritis, and several viral disorders. To date, we have evidence that it is a potent anti-inflammatory-anti-oxidant with anti-atherosclerotic and anti-cancer effects (see reference 20 for cross reference). Curcumin promotes wound healing and tissue repair. It controls over-reactive inflammatory reactions and improves inflammatory bowel disorder, peptic ulcer and gall stones. Turmeric/curcumin impacts blood lipid and platelet aggregation. The emerging scenario suggests that curcumin, given its multiple effects such as arrest of cell cycle, inhibition of signal transduction cascade and transcription factors (NF-Kappa-B), inhibits growth response gene, growth factors and oncogenes controlling cancer and metastasis<sup>21</sup>. Both curcumin and turmeric are antimutagenic antioxidants, protecting against DNA damage, promoting DNA repair, inducing xenobiotic drug metabolising enzymes (particularly the conjugating systems), promoting apoptosis, preventing angiogenesis and inhibiting telomerase. In keeping with its anticancer effects, it reduces, inhibits or delays tumours in skin, oral cavity, fore stomach, duodenum, stomach, colon, breast, prostate, liver, lung and ovary, and also has beneficial effects in blood cancer (leukaemia). Innumerable studies demonstrate its anticancer activity against many cancer cell lines. Thus curcumin is a potent preventive, and possibly even therapeutic, anticancer chemical agent, as it targets several mechanisms of cancer.

Curcumin has been shown to offer protection against ischemic injury to the heart, chronic inflammatory lung diseases, radiation damage, hyaline membrane disease in pre-term infants, pancreatitis, cystic fibrosis, inflammatory bowel disease, multiple sclerosis, Alzheimer's disease, toxicity due to pesticides and aflatoxin, renal injury due to drugs and toxins, scleroderma, hepatotoxicity and fibrosis. It even counteracts muscle injury and stress responses. Oxidative damage to the lens of the eye resulting in cataract is ameliorated. Diabetes and its complications are also reduced. The various effects of curcumin are mainly due to its antioxidant, anti-inflammatory, antiproliferative and antifibrotic effects. It has anti-bacterial, anti-

fungal, anti-viral (AIDS & HPV) activity as well (See ref 20 for cross references). However, most of the studies have been either *in vitro* or *in vivo* in animals. Even though curcumin has several biological effects, its pharmacokinetics show a poor bioavailability, and large doses are needed for clinical trials. Oral administration of turmeric and curcumin is well tolerated.

Several trials, albeit not very well designed, have been carried out with positive results (see reference 20 for cross references). The very first clinical study was in India, and it was aimed at assessing the anti-inflammatory effects of 1200 mg of curcumin in patients with arthritis. The clinical symptoms of arthritis were ameliorated. Similar was the observation with respect to post-operative inflammation and idiopathic orbital tumors. Observations in cancer with turmeric extracts for local applications indicated positive response, in studies carried out in India and in Taiwan<sup>22</sup>. Patients with submucous fibrosis and oral leukoplakia showed clinical improvement and reduced micronuclei in oral cells<sup>23</sup>. Turmeric 1-1.5g/d in reverse smokers reduced pre-cancerous lesions on the palate as well as DNA adducts and micronuclei in oral epithelial cells<sup>20</sup>. In subjects with colon cancer, a dose escalation study did not exhibit any toxicity, and CEA and COX2 levels were reduced<sup>24</sup>.

Recent clinical trials have yielded some positive results. Patients with pancreatic cancer who received 8 gm/day of curcumin orally for two months were evaluated for response and for toxicity. Four patients had stable disease (2+, 2+, 3+ and 7 months) and one patient had a brief partial remission (73% reduction in tumour size) that lasted one month. No toxicities were observed<sup>25</sup>. Curcumin was well tolerated, and this preliminary clinical trial suggests biologic activity in pancreatic cancer.

In multiple myeloma patients, curcumin in doses of 2-12g/d, was able to downregulate NF- $\kappa$ B, STAT3 and COX2. The authors draw the conclusion that there is a potential therapeutic role for curcumin, that should be further investigated either alone or in combination with other active agents as a modulator of chemo-resistance<sup>26</sup>. Preliminary studies are being undertaken with curcumin in patients with Alzheimers disease and those with cystic fibrosis. In an open trial, turmeric administered in the form of 300 mg capsules was found to cure peptic ulcers. Curcumin is also documented to have antipsoriatic activity in humans (See 20 for cross references,) Thus, in the near future, turmeric/curcumin will be recognised as a nutraceutical. Despite its poor bioavailability it can be used in India in higher quantities along with food to help in the prevention of a variety of disorders.

Though there are several substances/ingredients which seem to impact the cancer processes, as on date we are far from having firm evidence based on science to guide policy decisions. Nonstarchy vegetables probably protect against upper aerodigestive cancers. Foods containing beta carotene and vitamin C probably protect against oesophageal and lung cancers<sup>27</sup>. Similarly, allium vegetables (garlic) and fruits probably protect against stomach cancers. Folate-containing foods probably prevent pancreatic cancers. Foods containing dietary fibre, garlic, milk, and calcium probably protect against colorectal cancers. Foods containing lycopene and selenium, and selenium

supplements, probably prevent prostate cancers. In *in vivo* experiments, herbs and spices such as saffron, ginger, pepper and spice mixes are biologically potent as cancer-preventing agents. Only future studies in humans can throw further light. Nevertheless, one can recommend foods containing these to be consumed as dietary supplements<sup>28</sup>.

### **Coccinia indica**

*Coccinia indica* (ivy gourd), belonging to the Cucurbitaceae family, has been widely used in the traditional treatment of diabetes mellitus in India. In a double-blind, randomised placebo-controlled study in newly detected diabetes (type 2) patients, an alcoholic extract of 1g (equivalent to 15g wet weight) of leaves and fruits induced a hypoglycaemic effect within 90 days of treatment. Both fasting and post-prandial blood glucose fell by 16 and 19%, respectively, with lowering of glycosylated Hb. No other alterations in anthropometry or blood lipids were observed<sup>28</sup>. The ingredients present in the extract of *coccinia indica* such as triterpenes, probably act like insulin, correcting the enzymes of the glycolytic pathway and enhancing lipolysis. As a common vegetable in Indian cuisine, it can be an excellent adjunct in diets for persons with diabetes.

### **Health claims, substantiation and regulations**

A health-related claim can be:

- a nutrient function claim,
- a structure/function claim (enhanced function claim),
- a health claim or disease reduction claim. However, some countries do not permit a disease reduction claim (eg. Malaysia). “Functional food” was a term that was first proposed by the Japanese scientific academy. Subsequently it was changed to “Foods for specified health use” (FOSHU), and an attempt was made to pass legislation requiring that its efficacy be described on the label<sup>29</sup>. Appropriate randomised clinical trials need to be carried out in subjects/patients for whom the food is indicated, with necessary markers and statistics. Guidelines have been set for clinical trials.

The “Functional Food Science in Europe” (FUFOSE) project defines a functional food as one that has been demonstrated to affect one or more target functions in the body. On the basis of evidence-based medicine, randomised, placebo-controlled, double-blind trials are to be carried out for recommendations at population level. ILSI Europe set up a project “Process for the Assessment of Scientific Support for Claims on Foods” (PASSCLAIM) which started with FUFOSE, and built upon the principles defined within the publications arising out of the FUFOSE project<sup>30</sup>. It selects common criteria for how markers should be identified, validated and used in well-designed studies to explore the links between diets and health claims. The development of functional foods should be based on a sound scientific knowledge of the target function in the body and the demonstration of effects relevant to improved health or reduction of disease risk. The project identifies foods based on evidence from human studies using markers relating to biological

response or on intermediate endpoint markers of disease, as being capable of providing a sound scientific basis for messages and claims about functional food products. It says that it should examine the existing legislation and dietary guidelines, review the evolving science; and make it comprehensible to consumers. The food or its ingredient should be characterised, and substantiation should be based on well-designed studies in humans comprising the target group for a sufficiently long duration so as to elicit a response. When end-points cannot be defined, appropriate biomarker(s) should be identified and used as intermediate endpoints. A relevant biomarker is a well-defined biological, physiological, clinical or epidemiological indicator. Ingestion of the food, food constituent or ingredient should modify the specified biomarker for which there is a relationship between and the state of health and the measured parameter. A claim should be scientifically substantiated by taking into account the totality of the available data and after weighing all the evidence.

It is very important to define and implement rigorous, standardized manufacturing stages/procedures, quality assurance and quality control techniques. In the case of dietary supplements, the FDA in the US permits a qualified health claim based on emerging evidence of substance/disease relationships. In India, the recent Food Safety and Standards Act<sup>31</sup>, which is yet to be implemented, provides that all functional foods/health foods/nutraceuticals have to be approved by a special panel.

## **Conclusions**

The concept of functional foods has been accepted internationally. While literature is full of reports of the benefits of food ingredients, the strength of evidence ultimately lies in deciphering the role of specific diets or culture-specific patterns with documentation of diseases and risk factors in the groups concerned. Genetic polymorphisms can complicate the issue. In sub-populations, results may vary. Randomised trials, regional differences and cross-country trials may provide the final answers. Well-designed intervention studies can go a long way towards a prescriptive approach. It is also important to realise that effect size may be small and benefits may be seen after long periods of time. Although these foods are known by different names-nutraceuticals, dietary supplements, or functional foods, they hold significant promise in the promotion of human health and disease prevention. However, health professionals, nutritionists, regulatory toxicologists and government regulatory bodies should work together to plan appropriate regulations to provide the ultimate health and therapeutic benefits to Mankind. One should keep in mind a remark attributed to Paracelsus (1493–1541 AD): “the dose makes the poison”. The right dose differentiates between the remedy or cure, and toxic/adverse reactions.

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# THE RECENT WHO/FAO/UNU REQUIREMENT PATTERN FOR INDISPENSABLE AMINO ACIDS AND THEIR IMPLICATION FOR PROTEIN QUALITY

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## Introduction

The previous international estimates of indispensable amino acid (IAA) requirements in humans at various ages were set out in the 1985 report of the Joint

FAO/WHO/UNU Expert Consultation on energy and protein requirements<sup>1</sup>. In the last two decades, an expanding body of evidence has

Amino Acid	2008 FAO/WHO/UNU		1985 FAO/WHO/UNU	
	mg/kg/d	mg/kg	mg/kg/d	mg/kg
Isoleucine	20	30	10	15
Leucine	39	59	14	21
Valine	26	39	10	15
Lysine	30	45	12	18
Methionine + Cysteine	15	22	13	20
Phenylalanine + Tyrosine	25	25	14	21
Threonine	15	23	7	11
Tryptophan	4	6	3.5	5
Histidine	10	15	8-12	15
TOTAL IAA	184	277	93.5	141

emerged to suggest that the requirements of IAA are probably higher than previously thought. A review of these data led a recently constituted WHO/FAO/UNU Expert Committee to recommend, in the case of adult humans, the use of revised indispensable amino acid requirement values<sup>2</sup>, which are about two to three times higher (Table 1) than the earlier international recommendations<sup>1</sup>.

The earlier estimates<sup>1</sup> of IAA requirements for adults were so low that it would have been possible to achieve adequate intakes of IAA's from any diet (Table 2). Indeed, dietary protein quality in this case would be of little practical consequence for adult human protein nutrition.

Amino Acid Score based on			
Protein Source	Lysine Content <sup>1</sup> mg/g protein	1985 WHO/FAO/UNU (18 mg/g protein) <sup>2</sup>	2008 WHO/FAO/UNU (45 mg/g protein) <sup>2</sup>
Wheat	27	>100	60
Rice	35	>100	78
Sorghum	24	>100	53
Millet	22	>100	50
Nuts / Seeds	35	>100	77
Vegetables	43	>100	96
Legumes	73	>100	>100
Animal Protein	82	>100	>100

<sup>1</sup> Reference 50,51; <sup>2</sup> Table 1

## Methodology leading to the new requirement

The need for a re-evaluation of the IAA requirement was based



- on the inadequacies of the method of measuring IAA requirement from estimations of nitrogen balance<sup>3</sup>, and
- from initial thoughts and experiments based on short-term tracer studies<sup>4,5</sup> and predicted obligatory amino acid losses<sup>6</sup>, driven by the work of Vernon Young.

In the first case, the nitrogen balance method, as used in the classical studies of Rose, was flawed in terms of the excessive energy intake that the subjects received and because the miscellaneous nitrogen losses were not measured. Re-evaluations of the original N balance data by other investigators<sup>7</sup>, for example for the evaluation of lysine intake in which corrections for the miscellaneous N loss were made using either 5 or 8 mg N/kg/d, by Hegsted<sup>8</sup>, Millward<sup>9</sup> and Rand and Young<sup>10</sup>, have suggested higher lysine requirements, although the degree of difference in the amino acid requirement estimate was dependent on whether an allowance of 5 or 8 mg N/kg/d was made. The same applied for other amino acids as well. The N balance technique is also prone to severe error from the assumed value of the miscellaneous loss, because the slope of the N balance – amino acid intake curve is so shallow near the zero balance point that small differences in the values assumed for miscellaneous loss will have a large impact on the intake of amino acid required for equilibrium. Therefore the remaining uncertainty was sufficient to preclude the use of these data as a primary source for deriving IAA requirements.

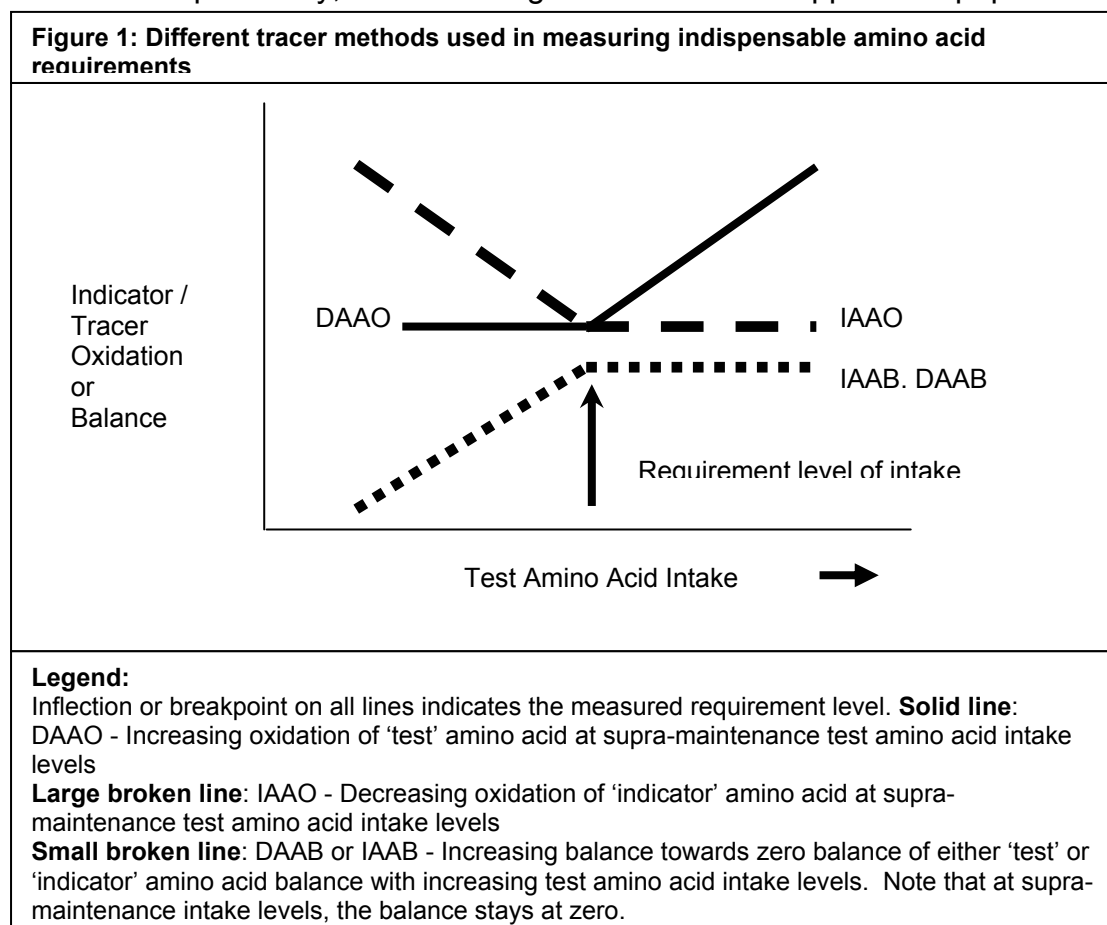
In the predicted obligatory amino acid losses model, the basal rate of N excretion in persons receiving a zero or very low protein diet was used to estimate the requirement for specific amino acids by relating it to the amino acid composition of body protein. The obligatory loss of nitrogen will be determined by the individual amino acid with the highest rate of obligatory loss relative to its concentration in protein. The other amino acids would be released based on their concentrations in the protein that is broken down, and oxidized based on the amount that is in excess of their requirement. This is a derivative method, which relies on relating the mean value of the obligatory N loss to the amino acid composition of mixed body proteins that are broken down, along with an assumption of the efficiency of utilization of dietary amino acids, to provide an estimate of indispensable amino acid requirement<sup>6</sup>. Because of its theoretical nature, this method could not be considered for providing primary data; however, these calculations and reports led to a sustained effort to accurately measure IAA requirements, which in turn resulted in a paradigm shift in the approach to measuring the IAA requirements of adults.

The current method of choice in estimating the IAA requirement is by the measurement of daily test amino acid balance (24h intake – 24h irreversible oxidation) using a stable isotope tracer amino acid technique, with different levels of the test amino acid being fed to adult human volunteers. The minimum level of intake of the test amino acid that results in a zero balance is considered to be the daily requirement of that amino acid. An important requirement of this tracer-based technique is the precise determination of the rate of test amino acid oxidation. This in turn requires precise measurements

of the isotopic enrichment of the pool directly supplying substrate for oxidation, and this is difficult to determine for most amino acids, except leucine<sup>11</sup> and probably methionine<sup>12</sup>.

However, the kinetics of leucine are well established<sup>13</sup>, and allow for a direct determination of leucine balances over 24 hours. The 24h balance method has been validated<sup>14</sup>. Earlier short-term tracer balance studies had shown that the daily requirement for leucine was greater than the 1985 FAO/WHO/UNU value of 14 mg/kg/day and was probably ~40 mg/kg/d<sup>3, 4</sup>. One of the arguments against the short-term amino acid oxidation studies was that they were done over a few hours, with extrapolations to a 24h day; it is possible that variations in the rate of leucine oxidation at different periods of the day would not allow these extrapolations to be easily made. A significant development in this field was made by Young's group, using a demanding 24h tracer balance protocol after adapting subjects to their experimental diets (or levels of test amino acid intake) for one week<sup>14, 15</sup>. These 24h direct amino acid balance studies confirmed that the leucine requirement was almost 3 times as high as the earlier estimate<sup>1</sup>.

These findings of a higher leucine requirement in young, well-nourished American men had not been validated in populations from different areas of the world. Specifically, these findings needed to be applied to populations



from developing countries, in whom there may be adaptations to lower-than-normal protein or leucine intakes, thereby reducing the daily leucine

requirement. We studied the leucine requirements of healthy, well nourished Indians using the 24h daily amino acid balance (DAAB) technique with L-amino acid mixtures (that supply graded levels of leucine) given to the subjects for an adaptation period of one week<sup>16</sup>; the requirement for leucine was set as the level at which there was a zero leucine balance (Figure 1).

It is worth remembering that ~ 50% of the adult population in India was chronically undernourished according to a body mass index (BMI) standard of 18.5kg/m<sup>2</sup><sup>17</sup> as a defining cut-off. Therefore, an additional study was undertaken to assess the leucine requirement of chronically undernourished young Indian men, using of the same 24h DAAB technique<sup>18</sup>. Both these studies confirmed the finding of earlier short-term studies that had indicated a higher leucine requirement.

These developments in tracer methods really meant that one could measure the requirements of leucine with some certainty. However, could the requirement of the other IAAs simply be taken to be similarly higher, or, could the requirements of the other IAAs be independently and experimentally confirmed? The key problem was in the measurement of the precursor pool of the tracer amino acid, since this was critical to the measurement of the amino acid oxidation. A more recent technique (that had its roots in earlier animal experiments) that really broke the impasse in experimentally measuring the requirements for all the other IAAs was the indicator amino acid oxidation technique (IAAO). In this method, the test amino acid and the tracer amino acids are different, the nature of this difference being such that the behaviour of the tracer oxidation and balance under different test amino acid intakes determines (or indicates) the test amino acid requirement. In this approach, the oxidation and balance data of the indicator amino acid (whose intake is held constant) at different test amino acid intakes can be analysed to yield a breakpoint of a plateau in indicator amino acid oxidation (IAAO), or a zero balance (IAAB), which indicates the requirement of the test amino acid (Figure 1). This is because, at suboptimal (limiting) intakes of test amino acid, protein synthesis is 'frustrated' leading to increased oxidation of the other IAAs. At intakes of test amino acid that are optimal or above, the indicator amino acid oxidation would plateau off at its lowest level, and its balance would fall to zero (Figure 1). In general, the technical problems of precursor pool identification that are related to the DAAO/DAAB method are not present in this method, since the indicator chosen is one in which the precursor pool is known and/or validated. This method is either applied as a short-term IAAO method<sup>19</sup>, or a longer-term 24h IAAO and IAAB method<sup>20</sup>. The requirement is set as the intake level that provides for an inflection (or breakpoint) in the pattern of the indicator amino acid oxidation or balance response to different test amino acid intakes.

The short-term IAAO method has been used with lysine or phenylalanine as the indicator amino acid<sup>21, 22</sup> wherein the appearance of the <sup>13</sup>C label (from the labelled amino acid) in the breath is measured after food intake, over the course of a few hours. Importantly, these studies are conducted after a short (48h) dietary adaptation period. The relative ease of the method, the short duration of dietary adaptation and the relatively non-invasive nature of

experimentation, are advantages that allows for many experiments at different levels of test amino acid intake to be carried out on the same subject. This, in turn, allows for the measurement of the variances of the requirement estimates for each amino acid. On the other hand, the lack of a sufficient dietary adaptation period, the lack of measurement under fasting conditions, and the short-term nature of the after-feeding evaluation may or may not influence the result of the amino acid requirement; there is insufficient evidence available at present to make a judgement about this.

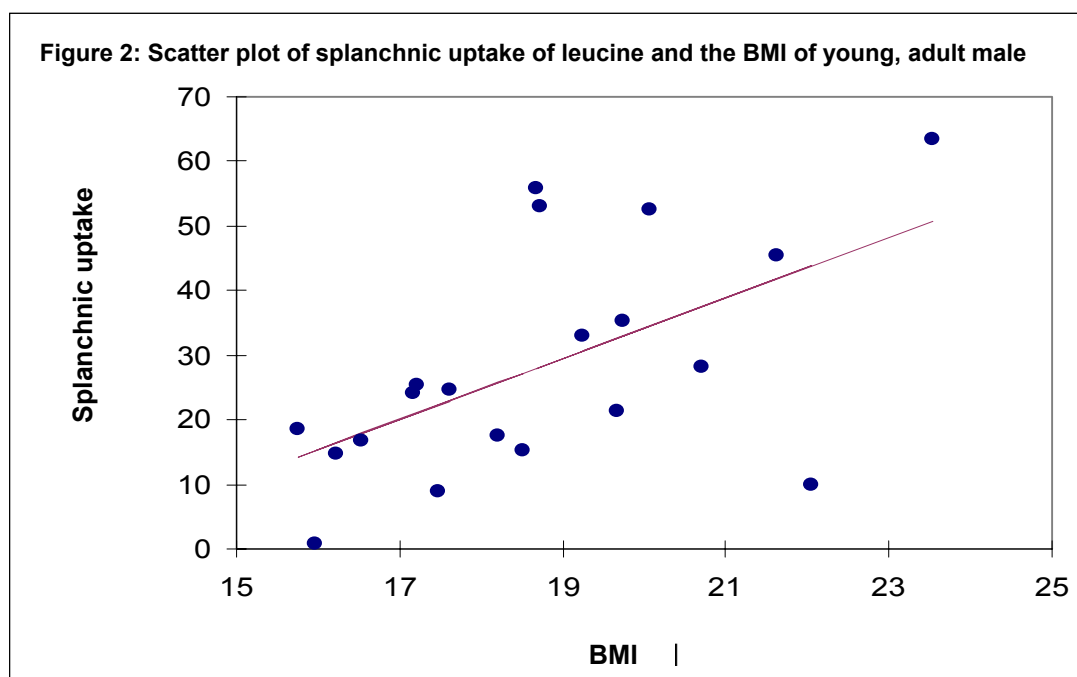
The longer-term, 24h IAAO and IAAB method<sup>20</sup> were developed using the kinetics of leucine as the indicator amino acid. In the case of leucine, there is no technical uncertainty about the adequacy of the method of measuring leucine oxidation and balance over a 24h period using a 12h fasted and 12h fed protocol. The output measures used for assessing the adequacy of a test amino acid intake include the 24h oxidation or balance, or a 12h post-feeding oxidation measurement. These measurements are performed after an adequate dietary adaptation period of one week, thereby removing the uncertainty about the measurement of the amino acid estimate in un-adapted or inadequately adapted individuals. The long-term dietary adaptation and 24h protocol render these experiments demanding, thereby restricting the numbers of studies that can be performed in a single subject. Nevertheless, these studies using the 24h IAAO or IAAB measurements with an adequate dietary adaptation period are considered to be the best available measurement for the determination of amino acid requirements. Based on the 24h IAAO model as the primary source of data<sup>20, 23-30</sup>, the recently constituted WHO/FAO/UNU Expert Committee on protein and amino acid requirements<sup>2</sup> recommended a generally increased pattern of IAA for adults (Table 1).

## Implications

These new recommendations have an implication for protein quality requirements. The actual requirement value for lysine that is now established has profound implications with respect to an assessment of the protein nutritional quality of diets, especially in developing regions, in which cereal-based diets supply the major proportion of the indispensable amino acid intake<sup>31, 32</sup>. Thus, it is evident that the populations at greatest risk of a dietary lysine inadequacy are those in developing regions of the world<sup>32</sup>. There is already increasing evidence that the quality of protein influences linear growth in children<sup>33, 35</sup>. On the other hand, it is also evident that populations that consume diets consisting largely of evidently poor quality cereal protein have survived quite effectively. Assuming that the new IAA requirements are correct, the question that remains is, are these populations physically and functionally healthy? Alternatively, was their possible adaptation to a low-quality protein intake “cost-less” or “costly”? Do they have potential contributions from gut microbes, of nutritionally significant amounts of IAA input, to supplement that coming from the diet?

The first two questions may be answered by correlating some criterion of health with IAA intake. For instance, the physical (anthropometric) characteristics and activity (functional) patterns of an individual could be used

to diagnose a state of Chronic Energy Deficiency. However, we do not, as yet, have an anthropometric, or functional criterion, that can be used to define a minimum but safe level of intake of IAA's. Populations consuming low lysine diets have been shown to have a lower level of selected immune markers as well as responses to stress<sup>36, 37</sup>, and in some cases, a relatively higher lysine intake over 3 weeks resulted in a slightly improved muscle function<sup>29</sup>. Clearly, more functional studies are required. Of concern, however, is the possibility



that the environmental and parasitic burden imposed on poorer, undernourished communities may actually result in a higher lysine requirement<sup>38, 39</sup>. Indeed, the splanchnic uptake of leucine is better in subjects with a higher BMI (Figure 2)<sup>40</sup>, indicating that gut function may well be an area of research in relation to the adaptive price paid by undernourished humans.

This would imply adaptation with costs, since it is likely that a large proportion of such populations, also subsisting on mainly cereal-based diets, would face the risk of deficiency. To answer the third question posed above, it is also possible that the gut microbes contribute significantly to intestinal lysine (and other IAA) intake. For example, there is evidence of significant absorption of essential amino acids synthesized by the gut microbes in simple-stomached animals and humans<sup>41, 42</sup>. From labelling experiments using <sup>15</sup>NH<sub>4</sub>Cl incorporation into microbial lysine in normal human subjects and ileostomates it has been estimated that microbial lysine absorption was 29–68 mg/kg/d, which is of the same order as the estimated average requirement of lysine (30 mg/kg/d) in human adults<sup>43</sup>. However, while this suggests that nutritionally significant amounts of microbially derived lysine are absorbed, the quantification of the amount absorbed is technically complicated by the need to estimate the <sup>15</sup>N enrichment of the lysine that is being absorbed, which seems to occur mostly in the small intestine<sup>44, 45</sup>. Using the indicator amino acid technique specified above, we have determined, through the reduction in leucine input into the body after antimicrobial treatment, to reduce the

intestinal microbes. Using this method, we were able to determine that the potential leucine (and by extension, other IAA) input from the gut microbiota was of the order of ~ 20%, and in the potential range of nutritional relevance<sup>46</sup>.

## **Protein quality**

Regardless of functional evaluations, or of alternative sources of IAA in the diet, it is possible to evaluate the protein quality in the diets eaten in developing regions. Protein nutritional quality can be measured in terms of an amino acid score. This concept, first introduced in 1946<sup>47</sup>, is now defined as the concentration of the limiting amino acid in the food protein as a proportion of the concentration of the same amino acid in a reference amino acid pattern<sup>48</sup>. Table 2 shows the reference amino acid pattern for the different reference patterns that have been recommended<sup>1, 2</sup>. The next step is to identify the limiting amino acid (having the least concentration in mg/g protein) in various proteins from different sources, and to use these amino acids in the consideration above. The identification of the limiting amino acid is derived from the ratio of the amount of the amino acid in 1 g of a dietary protein source to the amount of the same amino acid in 1 g of an ideal standard protein, or the reference pattern of IAA requirement<sup>2</sup>. The amino acid score can be made more accurate by correcting for digestibility of the protein source. Thus, the digestibility of mixed vegetable protein diets by Indian children may approximate 65-85%<sup>49</sup>. This method yields a new score, which is called the Protein Digestibility Corrected Amino Acid Score<sup>2</sup> (PDCAAS). While the digestibility factors may vary, this still gives a more accurate scoring pattern for proteins than earlier patterns. Lysine has been shown to be the most limiting in cereal protein, and in general, is at a much lower concentration in most plant foods<sup>50, 51</sup>. In addition, the lysine content of legumes is high, and their sulphur-containing amino acids are limiting, while animal foods have high concentrations of these amino acids, and are limiting in tryptophan. If the amino acid score is calculated for wheat flour, it would be >100 when the 1985 FAO/WHO/UNU amino acid requirement pattern for the adult is used as the reference pattern. This says that the nutritional value of wheat would be equal to that of high quality animal protein foods, such as milk, egg or meat, and there would be no concern with the assessment of the quality of plant protein in adults. On the other hand, for scoring purposes, if the recent 2007 WHO/FAO/UNU pattern were used, a relative nutritional quality of <50 would be obtained (Table 2). Therefore, a diet containing predominantly cereal as its protein source would be a cause for concern, as regards risk of lysine inadequacy.

It is worth considering the impact of this in the context of an Indian diet supplying 10% of the caloric intake as protein, which could come largely from cereal sources. For example, if a large proportion of the protein intake comes from cereals, and assuming a protein intake of 62 g (with a coefficient of variation of 20%), a cereal protein intake of 48 g, a legume (assuming that all non cereal plant protein was legume) intake of 10 g, and an animal protein (milk/eggs/meat) of 4 g per day, the lysine intake per day would be ~ 2400 mg (assuming cereal, legume and animal protein to contain 30, 64 and 85 mg

lysine/g protein respectively). For a 60 kg individual, the lysine intake would be 40 mg/kg/d. Further, assuming that this would be utilised to an extent of 70%, this would amount to the physiological equivalent of 28 mg/kg/d, which is just about the estimated minimum requirement for lysine. This also underscores the efficacy of legumes or animal protein in increasing the lysine content of the whole diet. For example, the ratio of cereal to legume in the above diet was about 80:20. In order to improve this diet and achieve a lysine intake of ~ 3000 mg/kg/d, a change in the cereal:legume ratio to ~ 60:40, would suffice. Therefore, a mix of different plant protein sources would be adequate to meet the desired lysine intake, even when the amount of animal protein in the diet is small or negligible.

One should not however, lose sight of the absolute need for dispensable amino acids and a utilizable source of non-specific nitrogen for the synthesis of the dispensable amino acids and other physiologically important nitrogen-containing compounds, such as purines and pyrimidines, glutathione, and creatine. The rate of formation of dispensable amino acids in the body appears to be determined by the total intake of nitrogen, and their requirement can increase when stresses such as infection exist. At lower levels of total nitrogen consumption the formation of adequate amounts of dispensable amino acids is impaired, and the critical limiting ability may be the ability to provide adequate amounts of glycine and glutamine<sup>52</sup>.

## Summary

In conclusion, protein quality is likely to be something that concerns nutritionists in India. For example, in a calculation of the risk of dietary protein deficiency based on a protein: energy (PE) ratio adjusted for protein quality or PDCAAS, it was estimated that, based on their habitual intakes, 23% of the sedentary adult male population of India could be at risk of IAA or quality protein deficiency<sup>53</sup>. Based on more recent data from tribal, rural and slum populations<sup>54-56</sup>, and recalculating the PDCAAS-adjusted PE ratio from these diets (excluding tribals whose diets are worse and constitute a special case), the risk of protein deficiency in elderly sedentary men and women was 34 and 45% respectively, and in younger adult sedentary men and women it was 8 and 14% respectively. Further, many of the reported diets (taken from NNMB surveys) were also suboptimal in micronutrients. For instance, in the tribal intake data, no less than 10% of the men and 30% of the women showed some *clinical* sign of micronutrient deficiency, and the NNMB report stated that their fruit and vegetable intake was "woefully inadequate". It seems impossible to quantitatively judge the optimal utilization of protein in these situations, and this is made more difficult since not all micronutrient intakes are energy-dependent. If it were possible to relate the PDCAAS-adjusted PE ratio to some functional or pathophysiological outcome, a much better definition of risk would be available, but that is very difficult to do. In addition, there are so many environmental hazards that it is difficult to pin down protein as the cause of suboptimal function or an adverse outcome; however, studies on lysine requirements in undernourished Indians before and after eradication of intestinal parasites<sup>38, 39</sup> would suggest that the environmental stresses are real.

Since the PE ratio has energy in the denominator, increasing this variable would inevitably reduce the requirement for a high PE ratio. The example of the sedentary individual is a case in point here: to satisfy this individual's reference PE ratio, one would have to drive protein intake upward, which would also result in an increased energy intake. This would inevitably result in higher energy intakes and fat accretion. It is tempting to speculate that this is one reason that there is a burgeoning obese population in India, but that argument would have to assume the existence of some protein-stat mechanism that drives appetite. However, from a public health viewpoint, it is worth inverting that reasoning to say that it is very important for the sedentary individual to lead an active life and exercise thereby increasing his/her energy requirement and lowering the required PE ratio to a more attainable level. Complementing cereal intake with high-quality protein sources is also a desirable and effective way to meet IAA requirements.

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# VITAMIN A SUPPLEMENTS AND MORBIDITY IN CHILDREN: A CONUNDRUM UNANSWERED?

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*It is a great pleasure to be involved in this small way, in recognizing Dr. Gopalan, his 90 years of life and his huge indescribable contribution to nutrition and health. He is a giant among nutritionists. For many decades he has made tremendous scientific contributions to the nutritional sciences, and has been both a general, but also in the front lines fighting in hundreds of ways to improve the nutritional status and health, particularly of children in India, and in the whole non-industrialized world. I have known this great man for over 45 years working in nutrition. Sometimes this has been in relation to nutritional controversies, which have divided our field. I have almost always been on Dr. Gopalan's side of the particular issue, which does not mean being in his camp, nor following his exact line. But as I indicate, below, in relation to vitamin A, I have believed, that underprivileged children should be getting most of this vitamin from food; I have questioned the conclusions of some of the vitamin A and mortality studies; and as described here I have been involved in research to show that mega doses of vitamin A supplements do not reduce morbidity from diarrhea or respiratory infections, although they do reduce morbidity associated with measles. I have been a strong proponent of children's rights including to be immunized against measles. As with Dr. Gopalan<sup>1</sup>, I have been strongly opposed to the enormously wide distribution of vitamin A capsules. I am also very concerned that a limited group of persons, can over these many decades, have captured enough power, funding and influence, to maintain the vitamin A supplementation programs in so many countries, often with support from UNICEF, WHO, The World Bank, NGO's, and of course bank rolled by the pharmaceutical industry.*

## **Introduction**

A long unanswered conundrum for those who both support widespread mega dose vitamin A supplements for young children, and who also believe that this reduces childhood mortality, is "why these supplements do not reduce morbidity except from measles?" A debate rages again on the issue of whether massive dose vitamin A supplements provided every 4 to 6 months in grossly unphysiologic doses actually reduces mortality<sup>2, 3</sup>. This topic has been reviewed many times. I have from the outset, like Dr. Gopalan<sup>1</sup> and his colleagues, been critical of some of the mortality studies, and have for many reasons not been an advocate of high dose vitamin A supplementation, especially in areas where serious cases of xerophthalmia and keratomalacia are now relatively rare. I have also, for decades, favored food-based approaches as being the best and most sustainable means of improving vitamin A nutritional status. Here I wish mainly to discuss the scientific evidence, which is rather consistent, in showing that other than with measles, vitamin A supplementation has no impact on morbidity, especially from diarrhea and respiratory infections. These are two leading causes of death in children 6-60 months of age in underprivileged populations.

Currently very large programmes exist to provide vitamin A supplements, usually in megadoses, to hundreds of millions of children in dozens of countries (including India) at a cost of millions of dollars. This vitamin A supplementation appears to have the support of WHO, UNICEF, The World Bank, the Gates Foundation, many large NGO's, the pharmaceutical industry and apparently is also supported (or at least "accepted") by the governments of many countries, including India. None of these "players" seem very much to consider the conundrum that death in children is usually preceded by morbidity. So even if these "players" have somehow been led to believe that vitamin A supplements markedly reduce young child mortality, the research shows no reduction in the incidence, nor the morbidity, of diseases that mainly cause these deaths. So on these grounds alone large dose vitamin A supplements are not justified. I have been a strong proponent of universal measles immunization. I believe that funds (including those now spent on vitamin A supplementation programs) would be better spent on total eradication of measles<sup>4</sup>.

### **The mortality studies**

By far the most influential study showing a major reduction in child mortality following vitamin A supplementation was that conducted in Indonesia<sup>5</sup>. The conclusions that children even without ocular clinical signs of xerophthalmia may be at an increased risk of death and that vitamin A supplements may decrease mortality by as much as 34 percent, was clearly important, if proved to be true. In the *Lancet* we immediately raised serious questions about this study<sup>6</sup>. We stated that randomization was not all done at the time of the baseline examination; that no placebos were used; and that despite randomization the control group at baseline had more clinical signs of vitamin A deficiency and poorer growth than the supplemented children. We pointed out that the units of randomization are villages but the data are presented for the point sampling units (children). We went on to point out that "no information is provided on cause of death." We concluded in the *Lancet*, "until the questions raised by us, and others, are resolved it would be premature to rush to action with vitamin A dosing in the belief that it will reduce young child mortality."

After the Indonesian research, the next most influential study showing a reduction in child mortality due to vitamin A supplementation was that done in India<sup>7</sup>. This helped stimulate a rush to the wide use of non-physiological high dose vitamin A supplements to whole populations. In the *New England Journal of Nutrition* we raised a note of caution stating that the problem is how best to ensure increased intakes of carotene and vitamin A to children at risk. This may be achieved by fortifying a suitable food and preferably in conjunction with better health care, nutrition education and horticultural activities to increase the availability of carotene-rich foods<sup>8</sup>. We stated: "Our major worry is that governments and international agencies may, as a result of recent research, only use vitamin A supplementation programs as a magic bullet to reduce childhood mortality, divorcing such programs from other efforts to improve nutrition and reduce morbidity. We cannot afford to ignore the underlying causes of malnutrition and infections, which may include

poverty and associated inadequate diets, unsatisfactory sanitation and water supplies, and uncontrolled infections. Attractive-sounding and well-motivated programs that are not sustainable must be avoided”

Only two vitamin A mortality studies were conducted in Africa. The first was by the Harvard University group in the Sudan. This showed no difference in child mortality between children receiving vitamin A compared with those not receiving it<sup>9</sup>. The second study was conducted in Ghana on a large population of children. There were 88 fewer deaths in the control population of children than in the vitamin A supplemented children. This was not a large difference, but was highly significant<sup>10</sup>. A piece in the *Lancet*<sup>11</sup> examined the findings and raised the still relevant question of whether the difference, in mortality might be due to measles. It is well known that measles presents with high fever, respiratory symptoms, and there is frequently diarrhea. As the causes of deaths in this study were “established by verbal autopsy (a wonderful oxymoron)” from mothers or relatives sometimes months after the actual death of the child, it is entirely feasible that many of the deaths recorded as due to a respiratory infection, diarrhea or fever (malaria) were in fact measles deaths. For example 23 percent of deaths were recorded as due to malaria, presumably based on a history of fever. Malaria can only be definitively diagnosed by identifying plasmodia in blood. So the fever could well have been due to measles not malaria. Similarly 26 percent of deaths in this Ghana study were recorded as due to “gastro-enteritis” presumably a history of diarrhea prior to death. Diarrhea is also a very common feature in measles; and measles presents with respiratory signs and symptoms.

A trial conducted recently in India compared death rates over a period of five years among nearly a million children, half of whom received high dose vitamin A supplements and half no supplementation. There was no significant difference in the death rates of those receiving the supplement compared with those not receiving it<sup>2, 12</sup>. In India, the Ministry of Health is stated to provide vitamin A supplements to about 55 million young children annually presumably on the questionable assumption that this would markedly reduce childhood mortality. An assumption strongly questioned over many years<sup>13</sup>.

### **Vitamin A supplementation and morbidity**

A detailed review was published in 1993 of eight major studies on the impact of vitamin A supplementation on young child mortality and this has had enormous influence<sup>14</sup>. It stated, “These studies together suggested that vitamin A supplementation resulted in an average reduction of 23 percent in mortality rates in children between 6 and 60 months of age.” That single statement has had an enormous influence in moving UN agencies, The World Bank, international NGO’s, and governments themselves, to implement programs to supplement young children with vitamin A. This “Beaton” report also stated: “In contrast to the very clear effect of vitamin A on mortality, we were forced to conclude that improvement of vitamin A status cannot be expected to impact on incidence, duration or prevalence of diarrheal and respiratory infections.” The Beaton paper went on to state “one aspect of the morbidity analysis that has direct relevance to field programs was the fact that

vitamin A intervention after the onset of measles impacted favorably upon the development of severe complications and reduced the case fatality rate.” So in reviews of these vitamin A supplementation studies in two African and several Asian countries, showed no impact on morbidity from diarrhea or respiratory infections, but markedly reduced the severity of the illness in measles, and lowered case fatality rates.

The obvious question to ask is if medicinal high dose vitamin A supplements reduce child mortality by 20-35 percent, then to what extent is this due to reduction in morbidity from diarrhea and respiratory infection (other than measles). Diarrhea according to WHO contributes to 32% and respiratory infections to 36% of child mortality (a total of 68%) in developing countries. Accordingly, we initiated studies in two countries to answer this very important question. These were conducted in Tanzania<sup>15</sup> and in India<sup>16</sup>. It is worth noting that (unlike most of the mortality studies reviewed by Beaton) our studies in Tanzania and India were true double blind placebo controlled clinical trials, and importantly we assured that all children were immunized (including against measles); we did not include seriously malnourished children, and all study children had access to reasonable health care. In neither study did regular vitamin A supplementation reduce morbidity from either diarrhea or respiratory infections. For the Indian study it was written “The differences in respiratory and diarrheal morbidity between the two groups were not statistically significant, and these findings remained unaltered after multivariate analysis”<sup>16</sup>.

There have been many studies done on vitamin A supplementation and morbidity. Almost all have shown no reduction in morbidity from diarrhea or respiratory infections as a result of vitamin A supplementation. Some have shown vitamin A supplementation increased morbidity from respiratory infections. In contrast several good studies have clearly demonstrated that vitamin A supplementation greatly reduces the severity of measles complications, signs of morbidity and case fatality rates from this important disease<sup>17, 18</sup>.

One of the more recent morbidity studies was conducted in Mexico to evaluate the impact of vitamin A and zinc supplementation on overall rates of childhood diarrheal disease and respiratory tract infections<sup>19</sup>. This was a double blind, randomized placebo controlled trial which included 736 children aged 6-15 months in periurban Mexico City. The subjects were assigned randomly to one of four groups namely

- vitamin A every two months,
- zinc daily,
- vitamin A and zinc, and
- placebo.

The children were followed for 12 months. The results showed that vitamin A supplementation in the four group analysis, was associated with a 27% increase in diarrheal disease and a 23% increase in cough with fever. Zinc decreased diarrhea in children under some circumstances. They concluded in

quote “vitamin A increases diarrheal disease and respiratory tract infections in young children in periurban Mexico City.”

A double blind randomized placebo controlled field trial was conducted in New Delhi in India to assess the impact of vitamin A supplementation on “morbidity from acute respiratory tract infections and diarrhea”<sup>20</sup>. In this study 900 children aged 9-60 months were studied. The conclusions were: “The study found the incidence and average number of days with acute lower respiratory tract infections to be similar in both groups. The incidence of diarrhea was also similar.” The paper goes on to state that “the incidence of measles was significantly reduced in the vitamin A supplemented group” when compared with those children receiving a placebo.

A WHO/CHD multicountry study published in the Lancet <sup>21</sup> looked at 9,424 mother infant pairs in Ghana, India and Peru. Fifty percent of mothers received 200,000 IU of vitamin A and their children received 25,000 IU of vitamin A at times of standard immunizations. The 50% in the control group received immunizations without vitamin A supplements. The conclusion was that the vitamin A intervention “had no effect on anthropometric status, or on overall, or severe, morbidity.”

Research in Indonesia<sup>22</sup> was conducted to evaluate the effect of simultaneous vitamin A supplementation on the immune response to measles immunization at 6 months of age. This was a randomized double blind placebo controlled clinical trial. It was found that “vitamin A administration reduced the likelihood of seroconversion to measles (after controlling for maternal antibody titers). The authors conclude “these results suggest that simultaneous high-dose vitamin A may thwart seroconversion to live measles vaccine in infants with maternal antibodies.” There are numerous other studies, almost all of which show that vitamin A supplements do not reduce morbidity, but the exception is that vitamin A does have an important role in reducing measles morbidity and mortality<sup>23</sup>.

## **Conclusions**

Reviewing the data relating vitamin A supplementation and its impact on morbidity and mortality, I can only draw one evidence-based conclusion. Vitamin A supplements reduce morbidity and mortality from measles. And clearly increasing vitamin A, or carotene intakes, will help prevent xerophthalmia. But despite the very dubious data showing that vitamin A supplements reduce childhood mortality, and the very conclusive evidence that it has no impact on morbidity from diarrhea and respiratory infections (with the exception of measles) we still see, in 2008 huge sums expended on vitamin A supplements. Why is this so? I have to conclude that many nutritionists, physicians and other players have been very uncritical. They have allowed one group of scientists, with one point of view, to set the agenda and to stifle other views. There is no need here to provide names. These “experts” took control of the International Vitamin A Consultative Group (IVACG) almost from its founding. The IVACG committee was appointed and run in a very undemocratic fashion. Some nutritionists labeled it this Group,

“International Vitamin A Capsule Group.” As a result of this dominance of the field food based approaches to control vitamin A deficiency have received too little attention, as have general measures to reduce hunger, to control infections, to improve health care and to prevent widening inequity almost everywhere. And we still have not assured that children receive their rights to be immunized against measles, let alone put in place measures to totally eradicate measles from planet earth

Note: This article is mainly questioning the use of vitamin A supplements in areas where serious xerophthalmia and blinding keratomalacia are now rare.

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# **GROWTH CHARTS FOR GROWTH MONITORING-WIDELY PROMULGATED AND EXTENSIVELY USED: HOW SUCCESSFUL ARE THEY IN REDUCING MALNUTRITION?**

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## **Introduction**

For most of the past four decades, growth monitoring (GM) of children has been practised<sup>1</sup>, and in some countries GM constitutes the major intervention to reduce malnutrition. It is often supported by the UN and bilateral agencies, by international NGO's, and by national governments. It is included in many of the heavily funded World Bank nutrition programmes such as those in Bangladesh, Ethiopia and Uganda. There are, of course, many other actions that donors and governments have supported to promote better growth of children<sup>2</sup>. However, concentration on support for GM, including the provision of weighing scales and growth charts, and funding for programmes to assist widespread weighing and charting have often remained a priority.

It is generally acknowledged that the GM movement began with the early work of David Morley in Nigeria, leading to the use of the innovative Ilesha growth chart<sup>3</sup>. Prior to that, of course, paediatricians and others in many countries were having babies weighed, and then followed their weight gain. Morley stressed the use of the chart to promote growth, and not to cure malnutrition. Growth monitoring (GM), based on the use of weight charts, has become extremely widespread in developing countries. A recent survey reported that 154 of 178 governments (88 percent) have growth monitoring in place<sup>4</sup>. In many of these countries, GM is the main, and most visible, activity for reducing malnutrition or for reaching the Millennium Development Goals of halving hunger by the year 2015<sup>5</sup>. Yet the most recent, 30-page comprehensive review of GM<sup>6</sup> states "there is no unequivocal evidence that growth monitoring is beneficial *per se*." Malnutrition, including stunting, remains extremely prevalent in many developing countries. A broad range of actions is needed to reduce this prevalence. We need to reduce inequity and in fact change the dominant world economic order, which widens the gap between rich and poor in almost all countries and also between countries. We need to accept that people have rights, as human beings, to health care, education and an adequate diet, and that the international community has obligations to help less privileged people gain these rights<sup>7</sup>. The objectives of this paper are to review, and then question, whether the wide use of growth charts, and programmes termed growth monitoring, although widely promulgated and extensively used, are successful in reducing malnutrition.

## **Growth monitoring and promotion**

The objectives of the weight chart, pioneered by David Morley in the village of Ilesha in Nigeria in the late 1960's, was to record the child's weight in a way that it was hoped would be understandable to the health worker, and also to the mother; and that this would then help to promote optimum growth<sup>3</sup>. Later, Morley the humble guru of growth charting stated that he accepted that

“mothers failed to understand the growth curve” and he also wrote that “growth monitoring, although successful in limited NGO situations, could not be shown to have an impact when spread nationally”<sup>8</sup>. As far back as 1984, I wrote<sup>2</sup> “The recording of a child’s weight on a growth chart in itself serves no useful purpose unless accompanied by some action. This has long been recognized, but in many growth-monitoring programs this is about all that is done. Under these circumstances the potential benefits of growth monitoring are not, and cannot be, realized.” We need to keep a clear sight of the fact that what is termed Growth Monitoring (GM) is really only weight monitoring. The importance of distinguishing acute from chronic malnutrition was demonstrated many years ago<sup>9,10</sup>. This led to the eventual acceptance of a classification of protein-energy malnutrition, and the current use of the terms stunting and wasting<sup>11</sup>, now usually based on Z scores.

Because height is practically never measured in GM Programmes (GMP), even if the health worker (often minimally trained) and the mother can correctly interpret the weight deficit in the child, neither of them can tell the nature of the low weight. For example a three-year-old child with very low weight could either be a thin wasted child of near-normal height with acute malnutrition, or a plump child stunted because of malnutrition and disease two years earlier, or something in between. Different actions or interventions may be needed in each of these instances. I suggested five operational rules, or guidelines if GMP were to have any chance of success<sup>12</sup>. These can be summarized as follows:

- infants should be enrolled in GMP as soon after birth as possible, because much of growth faltering begins in the first 12 months of life. so children enrolled in their third year (or even second year) will often have evidence of growth failure that is difficult to reverse, especially children who are stunted but not wasted;
- the health worker doing the weighing and charting needs to have adequate time (perhaps 10-15 minutes) for a dialogue with the mother, good communication skills and knowledge of factors that are likely to contribute to growth failure in children in the community, and feasible suggestions for action that can be given as friendly sensible advice;
- GMP should be integrated into primary health care (PHC). This is desirable because some of the advice given is likely to involve PHC (immunizations; ORT; family planning; etc);
- advice given should, as far as possible, be rather specific but provided as part of a dialogue helping to empower the mother to assist good growth in her child;
- GMP should be conducted in such a way as to make it most acceptable to the mothers, for example at times and locations most convenient for parents, rather than for health workers.

Despite some doubts about the heavy reliance on weight charts and their usefulness in promoting good growth, many of us suggested how GMP might be better done.

In the 1980’s, and subsequently, this rather simple-seeming intervention of GM became mired in international debate with strong proponents and

opponents. The literature on growth monitoring mushroomed, but almost all of this was in the form of opinions rather than evidence-based data. This became even more relevant as GM became the action in UNICEF's strongly supported and influential four-pronged so-called GOBI strategy<sup>13</sup> standing for growth monitoring, oral rehydration, breastfeeding and immunization. Again UNICEF was advocating growth monitoring as an effective, simple, and inexpensive way to prevent most child malnutrition. But this was being questioned because of the lack of evidence that growth charts are a better educational tool than health and nutritional education without growth charts<sup>14</sup>. Growth monitoring (GM) based on weight charts was getting reinvented as GMP, for Growth Monitoring and Promotion with increased realization that promoting good growth was an essential component. But advocates for reducing malnutrition in this way almost always linked growth promotion to the weight chart, and little consideration seemed to be given to growth promotion by different means without the use of a weight chart.

A recent detailed review of growth monitoring and promotion<sup>6</sup> states that "Growth monitoring may not be the best use of limited resources in countries with weak economies and inadequate health budgets: a limited package of health and nutrition interventions including good nutrition counseling may be preferable, aiming for good coverage and effective health worker performance, and prioritizing infants and children <18 months of age." But my visits to many countries, including as the leader of a UNICEF-appointed team to conduct a mid-term review of the heavily funded Joint Nutrition Support Program in Ethiopia, always showed me that few of these guidelines were followed, and it was abundantly clear that GMP, as practiced, could not possibly work to improve nutritional status. The concentration almost everywhere was still focused almost entirely on weight charting and not on growth promotion. Meanwhile, local situations, services and environments offered little to mothers to help them improve the growth of their children.

Increasingly, others including prominent journals like the *Lancet* were questioning the value of GM<sup>15</sup>. Importantly, a review was conducted for the World Health Organization (WHO) on the use of growth charts including in some large Asian countries where GM was a prominent activity. The conclusions<sup>14</sup> were generally critical, suggesting that growth data were often inaccurate, there was extremely poor interpretation of the recorded weights on the charts, practically no action was undertaken to initiate steps to maintain good growth and, importantly, GM was often isolated from primary health care or related programmes. The authors warned of the futility of pushing GM where the system could not make necessary changes, and against enthusiastic promotion of GM when it was destined to failure.

### **Evaluations of the effectiveness of growth monitoring**

Nutritionists, scientists and physicians frequently call for health interventions to be evidence-based. It is surprising that evidence showing any benefit of growth monitoring in improving the nutritional status of children is totally lacking. There have been no well-designed resilient studies showing that children participating in regular growth charting showed improvement in their

nutritional status to a greater extent than children not subjected to this, all other factors being equal. The recent comprehensive review on GMP<sup>6</sup> states that the most methodologically robust study to date is that of George and colleagues in South India<sup>16</sup>. That important study showed no additional benefit in terms of improvement in nutritional status due to the use of growth charts. The study was conducted in 12 intervention villages in Tamil Nadu. It was a collaborative study between the Christian Medical College, Vellore, and Cornell University in the USA. The 12 study villages were non-adjointing poor agricultural communities, each with a population of about 13,000. Growth monitoring had not been conducted in the villages before. Data showed that 70% of families lived in mud huts with one or two rooms; about 99.5% defecated in fields (not in a latrine); and less than 0.5% had kerosene or gas stoves. The 12 villages were divided into six “growth-monitoring package” of interventions (GMP) villages, and six “non-growth-monitoring package” of interventions (NGM) villages. NGM villages received the same interventions as GMP villages except for the growth monitoring. All the children in both groups received standard immunizations, were dewormed with albendazole, and had access to reasonable primary health care. In all the 12 villages a health worker provided health and nutrition education every two weeks. The health workers were locally recruited mothers who were given two months of training. So this research was mainly an evaluation to determine whether good GMP would have any greater impact on weight and height gain than the same interventions without the use of growth charts<sup>16</sup>. Comparisons were made by calculating monthly gains in weight and stature in the children in both groups in the 12 villages. The significance of differences observed was adjusted for age and gender. After 30 months of interventions, very similar improvements in growth were seen in GMP and NGM children. The interventions seemed to have improved the nutritional status of young children almost equally in both groups of villages. The data showed a lack of any additional benefit from growth monitoring over and above the benefit from the educational and other interventions, which both groups received. The growth charts did not seem to be a significant educational tool, because education with the use of the charts produced no better results than education without the charts.

Can GMP be carried out well and help to improve growth? Whenever GMP is criticized and doubt is thrown on its efficacy, those promoting it defend it by stating “yes it is usually badly done and thus ineffective, but if well done it really does reduce malnutrition.” The recent comprehensive review of GMP<sup>6</sup> summarizes evidence of the benefits of growth monitoring programmes to improve nutritional status in 15 countries. This starts with a review of the Imesi project in Nigeria, includes the Iringa project in Tanzania in the 1990’s, and ends with the current, much-debated World Bank-supported Bangladesh Integrated Nutrition Project (BINP). In many of these projects health and nutrition improved between the baseline and follow-up, but in none was it shown that the weight charts influenced improvements, rather than nutrition and health education, or other interventions such as immunizations, deworming, improved primary health care, attention to sanitation and water supplies, empowerment of women, maternal education, and others.

Perhaps the most quoted, as a good example (or even a successful example) of good GMP, was the Tamil Nadu Integrated Nutrition Project (TINP) in India in the 1990's<sup>17</sup>. TINP provided integrated health and nutritional services to nearly one million children in rural South India. In this project, growth monitoring was said to be used as an integrating strategy for providing a range of services including short-term selective supplementary feeding, ORT, immunization, deworming, vitamin A supplementation and nutrition counselling. A study was conducted to delineate the role of growth monitoring and its implementation in TINP<sup>17</sup>. This was not an evaluation of GM, but an attempt to examine carefully an efficient, relatively well-designed, very large project in which GM was a central focus. The GM part of TINP followed most, but not all, of the suggested operational rules<sup>12</sup> for successful GMP. One difference was that it did aim as much to “cure”, as to “prevent” malnutrition. The use of selective supplementary feeding was another difference. The results showed that TINP did, in general, improve the health and nutritional status of young children participating in the project. It cannot definitively be proved that the weighing and charting contributed, or contributed importantly, to the improvement in nutritional status. The weighing was used for selecting children to receive dietary supplements. TINP is a rare example of a programme in which indeed the weighing and charting were less important than growth promotion and activities such as maternal and child health care, health and nutrition education, and providing dietary supplements to selected nutritionally needy children. For this review the question is whether the weight charts were helpful, other than as a basis for selecting children to receive food supplements. Could the actions in TINP related to “promotion” have worked as well without the “weight monitoring”? That question cannot be answered.

The Bangladesh Integrated Nutrition Project (BINP), begun in 1996 and expanded in 2002, seemed at first to be producing good results, much of it claimed to be from successful GMP. It was initially funded with a US \$60 million loan from the World Bank to Bangladesh. Very large numbers of children aged 0-23 months in over 50 thanas attended growth monitoring sessions monthly at community nutrition centres. Supplementary feeding was available for children below  $-2$  SD of weight for age, apparently irrespective of their weight for height, because length and height were not measured. Hopes that BINP might prove to the world that well funded, and hopefully “good”, GMP could be successful seemed to be refuted. Save the Children (UK) evaluated BINP in 2002 and reported that the nutritional status of children 6 to 23 months of age was not significantly better in terms of weight for age in thanas in the project areas, than in carefully matched thanas that were not receiving project “benefits”<sup>18</sup>. It was also reported that fewer than eight percent of mothers in the project understood the particular BINP growth charts, and Save the Children (UK) strongly questioned both the ability and competence of BINP community nutrition staff, either to weigh children accurately, or to record weights satisfactorily, and most importantly to serve as nutrition and health educators<sup>19</sup>. Bangladeshi authorities and the World Bank refuted many of these findings.

## Conclusions

Using anthropometric measures, preferably both weight and height, to assess, or even follow the growth of children can be useful. But a review of the published reports and studies of growth monitoring leads to the conclusion that weight charts as used in most major GMP programmes have not been shown to be beneficial in improving growth and reducing malnutrition. Other means of promoting improved growth, especially of children under 24 months of age, have been shown to work, and many of these also improve the health and well being of the child. So it seems appropriate that those promulgating the use of growth charts would do better to concentrate on other ways to promote good growth in children at risk of malnutrition. Action to improve breastfeeding practices is one such measure. Malnutrition in young children is due to inadequate food, to lack of care, and to disease, often infections.

In their publication, Save the Children (UK) states: "*Thin on the Ground* "challenges the notion that trying to change the behaviour of poor mothers using growth monitoring and promotion will realize significant impacts on nutritional status. Our evidence suggests that too many mothers are too poor to act on their newly acquired knowledge about nutrition: they live in unhealthy, unsanitary environments lacking adequate and safe water; they have little or no access to health services; they are often illiterate; and they have inadequate time for childcare"<sup>19</sup>. It is difficult not to agree with this conclusion.

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# INDIGENOUS FOODS AND NUTRITION SECURITY IN INDIA: A CASE STUDY

Nandi<sup>1</sup> B K and Bhattacharjee<sup>2</sup> L

## Introduction

Understanding the food systems of indigenous peoples and the strengthening of these systems in the context of food security and nutrition is an issue of emerging importance. Existing knowledge warrants immediate action to promote the use of biodiversity in food security and nutrition programmes, as major steps towards the path of achievement of the Millennium Development Goals (MDGs). FAO's mandate provides a broad basis for conserving and using biological diversity in all its forms<sup>1, 2</sup>. It is unique to FAO that its policies and programmes on biodiversity are defined in agreement with its members. Given its broad mandate related to conservation and use of biodiversity, FAO is asserting global leadership in biological diversity for the international community.

Indigenous food systems offer a plethora of biodiversity for the diet and are good with respect to nutrition, positive dietary behaviours and other perspectives related to human well-being. There is little or no information specific for indigenous peoples (IP) from other countries. Government reports from India stress poor nutritional status (undernutrition) for Adivasis<sup>3, 4</sup> with stunting (63%) of children and chronic energy deficiency in adults (49% in men and 55% in women). Adivasis are at particular risk for chronic disease if obesity rapidly develops following increased access to poor quality foods and diets. There is need to promote food -based approaches that draw on indigenous food systems relevant to classic problems of hunger and nutrient deficiencies as well as to addressing the problem of non-communicable diseases. The following case study provides an overview of indigenous foods and nutrition security with an illustration of experiences of the indigenous food systems of the Bhil tribes. It will highlight:

- cultural orientation and community location of the Bhils
- food systems of the Bhils in Dang district
- potential of Bhil foods for food security with an emphasis on micronutrient contribution; and
- policy considerations for promoting indigenous food systems.

## Cultural orientation

Several tribes exist in different parts of India representing a good example of indigenous populations (IP) with a vast diversity in their culture, tradition and environment. There is a fairly rich habitat of natural foods in the tribal environment that needs to be positively exploited to promote their food

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security, nutrition and health. In India, IP are referred to as *Adivasis* (residents from earliest times), or the “scheduled tribes.”<sup>5</sup>. Generally perceived as oppressed within Indian society, there are more than 69 million Adivasis (7.5% of the Indian population) primarily in the mountain and hill areas of States, including in the hills of Gujarat. These locations were a result of invasions of the Indo-Aryan tribes more than 3,000 years ago which developed the Hindu caste system. Today, more than 95% of the scheduled tribes (which are not included in the Hindu caste system) live in rural areas, have low levels of literacy and other socioeconomic indicators, and are exploited<sup>6,7</sup>. The Bhils in India form a major indigenous group with substantial communities in Gujarat, Madhya Pradesh, Rajasthan, and Maharashtra. The interregional diversity of groups which consider themselves to be Bhils poses an anthropological challenge in itself and has been labelled as the “Bhil problem”.

### Community location

There are more than 40,000 Bhils located in 4 Indian States. Dang district, the centre of this project, is the smallest and poorest district of Gujarat State in Western India. It is an offshoot of the Sahayadri range (mountainous area) and traditionally it was known as Dandak or Dandakaranya, which is mentioned in the Ramayana. The Bhils in Dang district occupy a fertile area characterized as 66% forest and 34% agricultural land. Once important farmers and recognized as one of the oldest communities in India, the Bhils today are a marginalized tribal group, but they are now reclaiming their land in Gujarat with government support. Most Bhils have areas of landholdings that vary between 2 and 10 acres, but one-third of Bhil are still landless<sup>8</sup>. From a development standpoint, preserving the ecosystem diversity of the Bhil Adivasis to support their livelihoods and reduce vulnerability is an issue of emerging concern.

### Bhil Community food system

Food Category	Total
Cereals & Millets	8
Fish & seafood	9
Meat & meat products	6
Poultry	8
Vegetables	23
Fruits, Nuts & oilseeds	17
Pulses & Legumes	9
Roots & tubers	9
Total	89

Documentation of Bhil traditional food list (TFS) was carried out in an FAO – CINE<sup>3</sup> project in 2001-2002. The study included household food consumption and dietary assessment surveys (187 households), providing information on traditional food patterns, seasonal dietary habits, procurement and cost of production<sup>9</sup>. The Bhil occupy a rich

habitat and consume a diverse variety of domesticated animals, plants, small animals and local fish varieties. They employ methods of preparation and processing that are unique to the culture. Eighty-nine commonly consumed foods have been identified as composing the Bhil traditional food list (Table

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1). The foods have been classified based on their food groups. The detailed food list is given in Annexure 1.

### **Potential of Bhil foods for food security**

The food-related practices and patterns of the Bhil Adivasis are highly influenced by their traditions and environment. Gathering foods from the forest, hunting and agriculture are common methods of procuring foods. They are mainly dependent on traditional plant and animal food sources, which vary widely according to the region. From a development standpoint, preserving the ecosystem diversity to support their livelihoods and reduce vulnerability is an issue that needs to be addressed. Promoting the production and strengthening usage of potential micronutrient rich foods is seen to be invaluable in strategic actions to improve food security and nutrition including emerging health concerns.

It is observed that the Bhils eat more of protein-rich foods such as meat and poultry. There are 14 types of meat and poultry and 9 fish varieties consumed. This is due to the fact that most of the animals are easily available in the jungle, where they are hunted and killed for their meat. Fish are readily available in the ponds, and are also purchased. Nine types of pulses and legumes are widely consumed, and so are eight different kinds of cereals and millets. A variety of vegetables, consisting of 23 types, form part of their diet, and these include leafy vegetables. Seventeen types of fruits are eaten by them (Annexure 1).

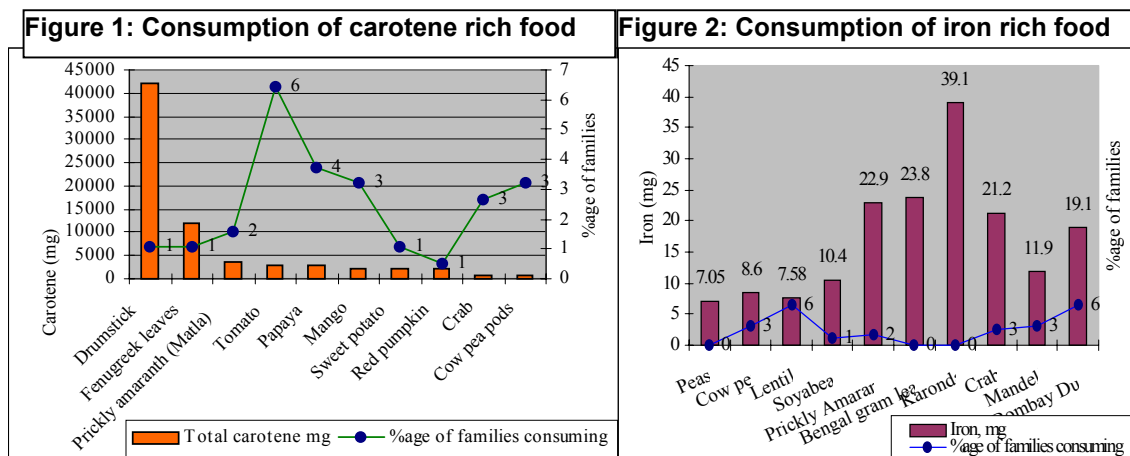
The Bhils cultivate their own vegetables and fruits on their farms and in their home gardens. The main crops cultivated are rice and ragi /finger millet (*Eleusine Coracana*) and, depending on irrigation facilities, other cereals and pulses are also grown. They also grow fruit trees such as mango, custard apple, guava, ramphal/ Bullocks' heart (*Annona reticulata*) and jackfruit on their farms. Wild fruits are also gathered in the jungle. Fruits are usually eaten in times of scarcity of food. The Bhils are very fond of eating fruits. During summer they eat amla/Indian gooseberry (*Emblica officinalis*), jackfruit, ramphal, banana and mango. Of these, mango, jackfruit, ramphal and banana are grown in home gardens (by those who have more than four acres) and timbroom fruit (wild fruit that is not listed in the Food Composition tables) is brought from the jungle. During the monsoon they eat jamboo (*Syzygium cumini*), banana and bamboo shoots. In winter they eat bore/Indian plum (*Zizyphus jujube*), amla, custard apple, guava and banana. Amla is procured from the forest and the other fruits are grown in their home gardens or farms. Papaya is often grown throughout the year in the home garden.

### **Nutrient composition**

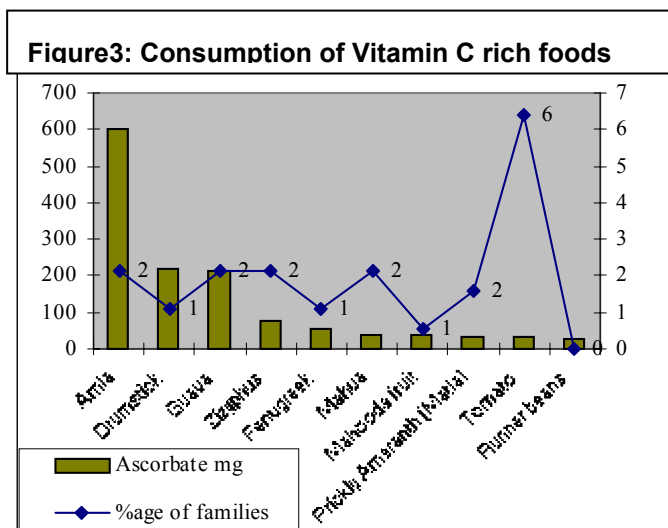
The nutrient compositions of certain foods were not available in the Tables in "Nutritive value of Indian foods". But they have been included in the list because they were an important part of the diet of the study group. In order to determine the foods normally consumed, data were collected through field visits and a rigorous food consumption survey. Seasonality, procurement of

food and cost of food production were also documented. These data are presented in Annexure 2 Nutrient values of all the foods were calculated using the Indian Food Composition Tables<sup>10</sup>.

### Inter-relation between micronutrient rich foods and consumption pattern



The top ten foods rich in total carotene picked from the traditional food list were analyzed. Figures 1, 2 and 3 show the graphical representation of these foods and the percentage of families consuming them. Tomato, papaya, cowpea and crab were the most frequently eaten foods amongst the carotene-rich foods. Though drumstick leaves and fenugreek have the highest in carotene content, only 1% of the study group consumed them.



Among the iron rich foods, lentils and Bombay duck were consumed by 6% of the families; followed by mandeli fish, cow pea and crab, each of which was consumed by 3% of the families. Karonda was the highest in iron content (but was not eaten by any in the study group), followed by green leafy vegetables such as Bengal gram leaves and amaranth. Among the Vitamin C-rich foods, tomato has a fairly low content of Vitamin C; however, it had the highest consumption in the study group (6%). Other sources of Vitamin C such as amla or gooseberry, which is the highest in Vitamin C content, showed a poor consumption pattern with only 2% of the group consuming it.

### Food preservation practices

Food preservation helps to increase the shelf life of foods and thereby increase the food supply. It helps to avoid food spoilage and wastage. The Bhils adopt traditional methods of food preservation<sup>11</sup>. Because of the absence of electronic gadgets such as refrigerators to preserve food for short

periods, the food prepared is generally consumed within the same day or at the most finished the next day for breakfast. Harvested foods also need to be preserved for periods of drought or scarcity. Bhils use different ways of preserving foods, the most common being drying, roasting and using cow-dung manure. Some of the examples include preservation of Karsani niger seeds in bamboo baskets which are coated with cow dung manure. These containers vary in size depending on the produce available. The coated containers are left in the sun to dry and then filled with the seeds. The manure helps to repel any insects from infesting the seeds. Foodstuff such as rice, varai and pulses are also preserved this way. A few educated families occasionally use neem leaves to preserve rice. Fire ash is also used as a preservative for pulses such as black gram and red gram. Generally no preservative is used for ragi because the red covering which is bitter in taste helps prevent infestation by insects.

Drying is probably the most effective way of preservation practised by the Bhils. Any extra numbers of fish such as muru and malya that are caught are first roasted over a hot plate or tava and then dried and kept to be consumed within a couple of days. Excess meat is generally dried by piercing it with sharp bamboo knives and then barbequing it over the fire. Once it is well heated, it is stored by wrapping it in cloth and storing it in bamboo baskets. When required, it is taken out, cut into pieces and added to curries. Vasarta or dried mushroom is also dried and stored in baskets that are normally used for catching crabs. Pickling is not practiced by the Bhils. However ragi papads (or dried thin pancakes) are prepared through papad making schemes initiated by the zilla parishad for women. This is done by preparing a ragi batter and then rolling them out into thin round shapes, which are left to sundry and are then packed and marketed.

### **Policy implications**

The availability of a wide array of foods is evidence enough to indicate that the existing nutrient potential can be tapped for strategically reducing the risk of micronutrient deficiencies. The dietary deficiencies of energy, protein, iron and vitamin A can be addressed through a sound nutrition education strategy targeted at women and children. Specifically, the strategy would be to promote the consumption of a wide variety of foods from the available major food groups. Meat, poultry, seafood and pulses/legumes are main contributors of protein and iron in the Bhil diet, while a variety of available leafy vegetables and fruits contribute to micronutrients like vitamin A, folic acid, vitamin C, iron including the phytonutrients.

There is not yet a complete nutrient composition profile available of the foods that Bhils eat. It is also important to understand that in the rural environment in which the Bhils live, they have indigenous resources and local knowledge to ensure good nutrition and health status in the midst of extreme financial poverty. One of the challenges is to address the issue of the Bhil people's livelihoods while promoting the use of their local indigenous foods to improve the nutrition situation, particularly micronutrient malnutrition.

## Conclusions and recommendations

Although this is well recognized, there is need to strengthen and promote integrated home gardening through increased production and consumption of nutritious foods (indigenous leafy vegetables, fruits, herbs and spices and other foods) with an emphasis on foods rich in micronutrients. Many schemes for Bhil development have been implemented successfully<sup>12</sup> through NGOs such as the Child Eye Care Charitable Trust (CECCT). Community savings activities and government-linked schemes as initiated by the Government of India have been beneficial.

The knowledge base generated so far relating to the Bhil diet can be used to facilitate food-based nutrition and health promotion programmes with a sustainable base of community-led activities. Improvement in food security, nutrition and health with implications for community-friendly policies and programmes can result in food security improvement outcomes that can impact on the nutritional status of the Bhils. It is recommended that:

- the use of biodiversity within food systems should be optimized within a contemporary context;
- indigenous knowledge on the values of food-based biodiversity and food processing should be documented;
- research to document the benefits of food-based biodiversity for evidence-based public policy and nutrition promotion should be validated;
- research would need to prioritize food analysis and the documentation of the composition of traditional foods, food processing of indigenous foods and minimizing anti-nutrient factors in indigenous foods, if any;
- commercial linkages are needed in developing and marketing traditional foods and for building rural / urban linkages;
- education, promotion and social marketing bring out the importance of indigenous foods to consumers. This can be targeted to key age groups such as children and adolescents;
- nutrition education should be mainstreamed in agrobiodiversity and horticulture programmes so as to address challenges related to promoting/enhancing consumption of a varied diet including indigenous foods/ foods offering wide variety (biodiversity);
- strategic partnerships and multi-sectoral linkages (government level) need to be established to support and advocate the importance of traditional foods on a wider basis and to share experiences.

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<b>Bhil traditional foods (89 species/varieties)</b>					
<b>Scientific name</b>		<b>Common/English name</b>	<b>Local name</b>	<b>Seasonality**</b>	<b>Preparation</b>
<b>Cereals</b>					
1	<i>Eleusine coracana</i>	Ragi or Finger millet or African millet	naglano	March-June	Roti, bhakri
2	<i>Oryza sativa</i>	Rice (hand pounded)	chokha	January-December	Cooked
3	<i>Panicum miliaceum</i>	Common or Proso millet	varai	October-January	Cooked
4	<i>Pennisetum typhoideum</i>	Pearl millet	bajra	-	Rotli
5	<i>Sorghum vulgare</i>	Sorghum	jowar	April-August	Rotli, gruel
6	<i>Triticum aestivum</i>	Wheat	gahoo	January-December	Rotli, gruel
7	<i>Zea mays</i>	Maize or Corn	makka	August	Roasted or as such
8	-		kharai	August	Roti, bhakri
<b>Fish and seafood</b>					
1	<i>Carcharias</i> sp.	Shark	khari fish	-	Curry
2	<i>Coilia dussumieri</i>	Mandeli	mandli	November-June	Steamed with egg plant and potato
3	<i>Elops saurus</i>		river fish	June-September*	Curry
4	<i>Harpodon nehereus</i>	Bombay duck	bubla	-	Steamed, fried with vegetables
5	<i>Paratephusa spinigera</i>	Crab	karachala	June-December	Curry
6	<i>Thaleichthys pacificus</i>		small fish fry	-	-
7	-		bodiya river fish (ravas)	June-September*	Curry
8	-		kokil zinga fish	June-September*	Fried or curry
9	-		murua fish	June-September*	Curry with vegetables
<b>Vegetables</b>					
1	<i>Abelmoschus esculentus</i>	Lady's finger	bhindi	August-September	Vegetable curry
2	<i>Agaricus bisporus</i>	Mushroom	kukkagodugu	July-August	Curry, dry vegetable
3	<i>Amaranthus spinosus</i>	Prickly amaranth	matla bhaji	June-September*	Boiled vegetable
4	<i>Asparagus racemosus</i>	Asparagus leaves	satavari	Year-round	Boiled vegetable
5	<i>Bambusa arundinacea</i>	Bamboo	bamboo	June-September*	Pickled, boiled
6	<i>Carrissa carandas</i>		karonda	April-July*	Curry
7	<i>Chlorophytu</i>		ugat	August-September	Vegetable



	<i>m tuberosum</i>		phylli		curry
8	<i>Cicer arietinum</i>	Bengal gram leaves	chana bhaji	November-March	Vegetable curry
9	<i>Cucurbita maxima</i>	Red pumpkin	lai bhopla	October-December	Boiled vegetable, fried
10	<i>Dalbergia latifolia</i>		sisam	March-May*	Semi-liquid preparation
11	<i>Dictyophora</i> sp.	Bamboo mushroom	vasarta	June-July	Dried, curry
12	<i>Lagenaria vulgaris</i>	Bottle gourd	dudhi	January-December	Vegetable curry
13	<i>Momordica charantia</i>	Bitter gourd	karela	June-September	Vegetable curry
14	<i>Moringa oleifera</i>	Drumstick	saragvani sing	January-June	Vegetable curry
15	<i>Phaseolus coccineus</i>	Scarlet runner beans	lili papadi	October-January	Vegetable curry
16	<i>Solanum melongena</i>	Eggplant or brinjal	baingan	January-December	Curry
17	<i>Tectona grandis</i>		teakwood leaves	April	Curry
18	<i>Trigonella foenum gracecum</i>	Fenugreek	methi	November-February	Vegetable curry
19	-	Elangve leaves		March-May*	Boiled vegetable
20	-		loti	June-September*	Bhaji
21	-		mokha	December-February	Curry
22	-		sag tree	June-September*	Bhaji
23	-		terani bhaji	June-September*	Bhaji, dry with dhal
<b>Meat and meat products</b>					
1	<i>Bos taurus</i>	Cow	gai	June-September*	Roasted, curry
2	<i>Capra hircus</i>	Goat	bakri	January-December	Curry
3	<i>Lepus capensis-Leporidae</i>	Rabbit	sasboo	December-April	Curry
4	<i>Rattus norvegicus</i>	Rat	onder	November-March	Roasted
5	<i>Sus scrofa</i>	Wild pig	jungli bhund	November-August	Boiled, roasted, curry
6	<i>Varanus flaveceas (yellow) or Varanus bengalensis.</i>	Monitor lizard	ghorpad	Year-round	Curry
<b>Poultry</b>					
1	<i>Columbia livia intermedia</i>	Pigeon	kabotar	March-May*	Boiled and roasted
2	<i>Gallus bankiva murghi</i>	Hen fowl	murghi	March-May	Curry

3	<i>Haliastur sphenurus</i>	Whistling kite	samadi	March	Curry
4	<i>Picoides pubescens</i>	Downy woodpecker		March	Curry
5	<i>Psittaciformes</i>	Parakeet, Parrot	popat	March	Curry
6	<i>Strigidae</i>	Owl	ghuvad	March	Curry
7	-		chakvat	March	Curry
8	-		titar	March	Curry
<b>Fruits, nuts and seeds</b>					
1	<i>Achras sapota</i>	Sapodilla fruit	chiku	November-March	Fresh, ripe
2	<i>Aegle marmelos</i>	Bael fruit or wood apple	billa	November-December	Fresh, ripe, chutney
3	<i>Annona reticulata</i>	Bullocks heart	ramphala	March-May	Fresh, ripe
4	<i>Annona squamosa</i>	Custard apple or sweetsop	seetaphel	August-September	Fresh, ripe
5	<i>Artocarpus heterophyllus</i>	Jackfruit	phanas,	April - September	Fresh, ripe
6	<i>Bassia longifolia</i>	Mahua	mahvoda	June- *	Flowers used for making wine, dry seeds
7	<i>Bassia latifolia</i>		doli mahuda	-	Oil
8	<i>Carica papaya</i>	Papaya	papeeta	January-December	Fresh, ripe
9	<i>Cordia rothai</i>	Gumberry	gunda	March-May*	Pickle, chutney
10	<i>Emblica officinalis</i>	Indian gooseberry	amla	February-May	Chutney
11	<i>Ficus racemosa</i>	Wild fig	umbara	February-May*	Chutney, raw
12	<i>Lycopersicon esculentum</i>	Tomato	tomato	January-December	Boiled, in dhal
13	<i>Magnifera indica</i>	Mango, ripe	aam	February-May	Fresh, ripe
14	<i>Psidium guajava</i>	Guava	jamrookh	October-January	Fresh, ripe
15	<i>Syzygium cumini</i>	Indian black berry	jamboo	May-June	Fresh, ripe
16	<i>Zizyphus jujuba</i>	Indian jujube	bore	October-January	Fresh, ripe
17	-		kakad	February-March	Pickle
<b>Pulses and legumes</b>					
1	<i>Cajanus cajan</i> (2 var.)	Red gram (tender pods, dry seeds)	tuver	January-December	Dhal
2	<i>Dolichos biflours</i>	Horse gram	kulad	April-June*	Boiled, steamed
3	<i>Dolichos lablab</i>	Field bean	val papdi	Winter	Fried, steamed
4	<i>Glycine max</i>	Soybean	soyabea	January-December	Boiled,

	<i>merr.</i>		n		vegetable
5	<i>Lens Esculenta</i>	Lentils	masoor	January-December	Dhal, boiled
6	<i>Phaseolus aureus Roxb (2 var.)</i>	Green gram, whole seeds, split seeds	moong	January-May	Dhal
7	<i>Phaseolus mungo</i>	Black gram	udad	January-December	Dhal, steamed, ground, fried as fritter
8	<i>Pisum sativum (2 var.)</i>	Peas (Green tender, dry)	vatana	December-April	Dhal, steamed, ground, fried as fritter
9	<i>Vigna catjung (2 var.)</i>	Cow pea (pods, dry)	chowli, chowli sing	January-December	Dhal, steamed, ground, fried as fritter
<b>Roots and tubers</b>					
1	<i>Asparagus racemosus</i>		shatavari	June-September*	Boiled
2	<i>Amorphophallus campanulatus</i>	Yam or Elephant foot	suran	October-May	Boiled vegetable
3	<i>Chlorophytum borivillianum</i>	White musali bhaji	safed musali bhaji	June-September*	Boiled vegetable and roasted
4	<i>Colocasia antiquorum</i>	Colocasia	aloknala	June-September	Boiled vegetable
5	<i>Discorea esculenta</i>	Spinney yam	kankholi		-
6	<i>Ipomoea batatas</i>	Sweet potato	shakariya	October-May	Boiled, fried, grated
7	<i>Solanum tuberosum</i>	Potato	batata	January-December	Boiled, fried, grated
8	-	Red tuber	kand koychi	June-August	
9	-		jungli kand	June-August	Soaked, boiled and eaten with salt
* Seasonality of use rather than months harvested.					
** Seasonality may vary with variety					
- Data not available					

<b>Nutrient composition of Bhil traditional food (per 100 g of edible portion)</b>														
<b>Food items</b>	<b>Moisture</b>	<b>Energy</b>	<b>Protein</b>	<b>Fat</b>	<b>CHO*</b>	<b>Fiber (total)</b>	<b>Ash</b>	<b>Calcium</b>	<b>Iron</b>	<b>Copper</b>	<b>Zinc</b>	<b>Magnesium</b>	<b>Manganese</b>	<b>Phosphorous</b>
	<b>g</b>	<b>Kcal</b>	<b>g</b>	<b>g</b>	<b>g</b>	<b>g</b>	<b>g</b>	<b>mg</b>	<b>mg</b>	<b>mg</b>	<b>mg</b>	<b>mg</b>	<b>mg</b>	<b>mg</b>
<b>Cereals and grains</b>														
Pearl millet (Bajra) <sup>2</sup>	12.4	361	11.6	5.0	67.5	1.2	2.3	42	8.0	1.06	0.02	137	1.15	296
Sorghum (Jowar) <sup>2</sup>	11.9	349	10.4	1.9	72.6	1.6	1.6	25	4.1	0.46	1.60	171	0.78	222
<b>Vegetables</b>														
Junglikhand, cooked <sup>1</sup>	84	63	0.9	0.1	14.5	0.4	0.1	31	2.5	0.04	0.50	8	0.1	9
Junglikhand, raw <sup>1</sup>	81	72	1.4	0.3	16	0.8	0.5	10	0.8	0.08	0.30	18	0.1	33
Mokha leaves <sup>1</sup>	66.1	111	3.5	0.9	22.1	4.4	3	831	5.1	0.10	0.70	173	1.2	51
Teruna leaves <sup>1</sup>	89	34	1.8	0.8	4.8	1.7	1.9	230	0.9	0.10	0.30	48	2.0	55
Mushroom, dry <sup>1</sup>	22	272	20.6	4.3	37.8	11	4.3	94	79.4	1.40	6.10	147	2.4	487
Doli mahooda seeds <sup>1</sup>	9.8	559	9	44.4	30.9	3.4	2.5	64	7.3	0.50	1.30	88	0.6	153
<b>Fruits</b>														
Indian gooseberry <sup>2</sup>	81.8	58	0.5	0.1	13.7	3.4	0.5	-	-	-	-	-	-	-
Indian Jujube <sup>2</sup>	81.6	74	0.8	0.3	17	-	0.3	4	0.5	.12	.10	-	.17	9
*Carbohydrate <sup>1</sup> Nutritive value from NIN analysis. <sup>2</sup> Gopalan, G., Rama Sastri, B.V., Balasubramanian S.C., 2002. Nutritive Value of Indian Foods. National Institute of Nutrition. Indian Council of Medical Research. Hyderabad-500 007. India														

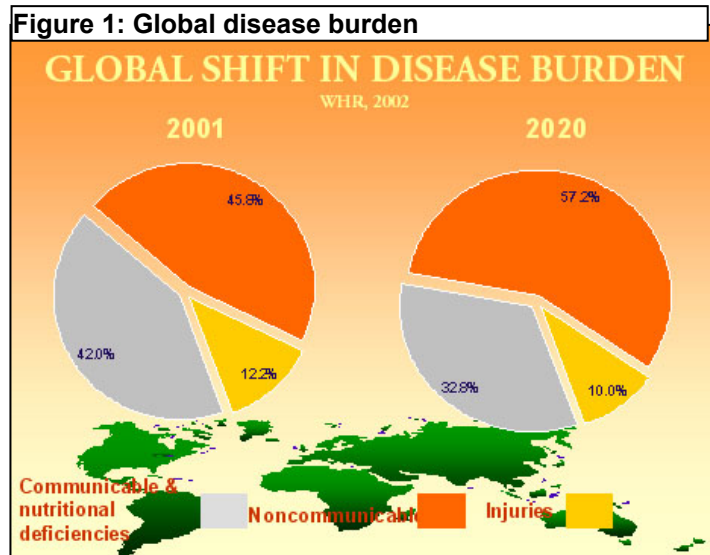
# A PRIMARY PREVENTION PARADIGM TO HALT CHRONIC DISEASE EPIDEMIC IN 21<sup>ST</sup> CENTURY INDIA

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## Introduction

Today, 79 % of all chronic disease-related mortality is occurring in developing countries. In fact, for adults below the age of 70 years in India, China and sub-Saharan Africa, the probability of dying from heart disease is already greater than for their Western peers<sup>1</sup>. Indeed, in the 21<sup>st</sup> century, India epitomizes the many developing countries facing epidemics of chronic diseases alongside persistent, though receding, diseases associated with poverty, such as nutrient deficiencies, infections and childhood mortality<sup>2</sup> (Figure 1).



## Nutrition and economic transition

As major economic and social development in recent decades has reduced malnutrition and infection-related infant mortality and enhanced child survival, a new brand of health problems has emerged among the rich, the middle class and the urban poor in India – increased susceptibility in adulthood to a host of respiratory, musculoskeletal and cardiovascular diseases, Type II diabetes, and other non-communicable lifestyle diseases (NCD)<sup>3,4</sup>. By the year 2020, mortality in India from communicable diseases, maternal and perinatal conditions, and nutritional deficiencies, is expected to fall from almost 5 million to below 3 million a year, according to the 1996 Global Burden of Disease series issued jointly by the World Health Organization (WHO), the World Bank and the Harvard School of Public Health. At the same time, deaths from non-communicable diseases (NCDs) and injuries in India are projected to almost double, from about 4 million to about 8 million a year<sup>5-7</sup>. India's new challenges in this century call for a new paradigm in confronting the onslaught of NCDs.

## Urbanization and sedentarism increased NCDs

Urbanization is a major culprit in the NCD epidemic worldwide. As economies develop, populations tend to migrate from rural areas to towns and cities, and

**Figure 2: Urbanized Indians adopt modern “affluent” heavv fat-sugar-salt-laden diet**



their health profiles change. Their reliance on plant foods diminishes. As evidenced in North America, Latin America and Central and Eastern Europe and Asia, affluence and status are equated with the adoption of a

certain “affluent diet”; high in meat, fat, and sugar and a lifestyle that includes high alcohol consumption and cigarette smoking and low levels of physical activity. While this influx of dietary energy helps to reduce the burden of malnutrition, the benefits of prosperity and improved health are compromised by the health risks of such affluent diets and poor lifestyle that historically accompany economic growth<sup>8, 9</sup>. The urban population in India has increased more than threefold in the past 40 years, from nearly 80 million to over 250 million at present. In 1995, the United Nations projected that by 2025, 50% of India’s population would live in urban areas<sup>10</sup>

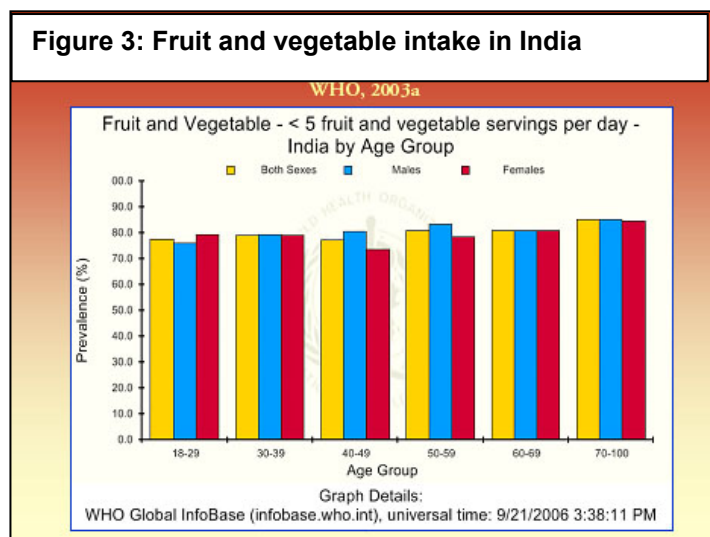
### Urban lifestyle and food patterns increase NCDs

This urban expansion coupled with increasing affluence, is leading to increased energy intake and changed food consumption patterns nationwide (Figure 2). For example, even a decade ago, the urban middle class was estimated to consume only 75% (326 g) of cereals per capita as the amount consumed by rural populations (465 g/capita), and to derive over 25% of calories from fats, oils and milk and milk products<sup>11</sup> (National Nutrition Monitoring Bureau, 1996). The wealthiest urban classes were estimated to derive up to 40% of their calories from fats as compared to 18.7% for rural adults, according to the available limited data.

### Intake of fruits and vegetables decreases

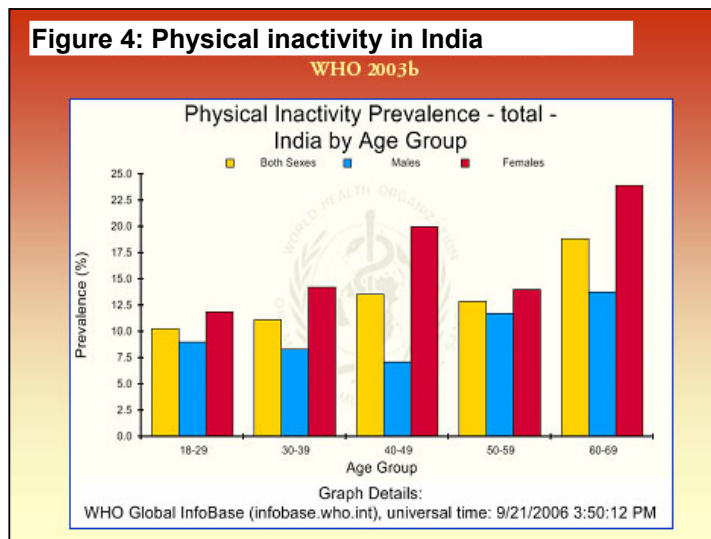
Although most Indians remain vegetarians, India’s National Nutrition Monitoring Bureau indicates that animal food intake has doubled over the past three decades among the urban middle class, and to a lesser extent in the rural population. In all sectors of society, the consumption of green leafy vegetables and other legumes remains

**Figure 3: Fruit and vegetable intake in India**



low, often below recommended levels<sup>11</sup> (Figure 3). According to a WHO sub-national survey of nearly 9000 adults in 2003, fruit and vegetable intake in the vast majority of Indians was below five servings/day in almost 80% and below 3 servings a day in about 50% of those surveyed.<sup>12</sup>

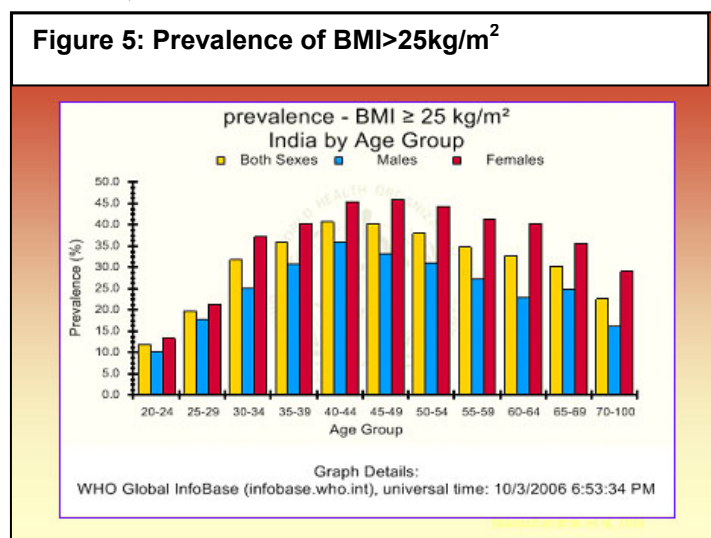
### Physical activity decreases



among middle-aged and older adults<sup>13</sup> (Figure 4).

### BMI rises above 25

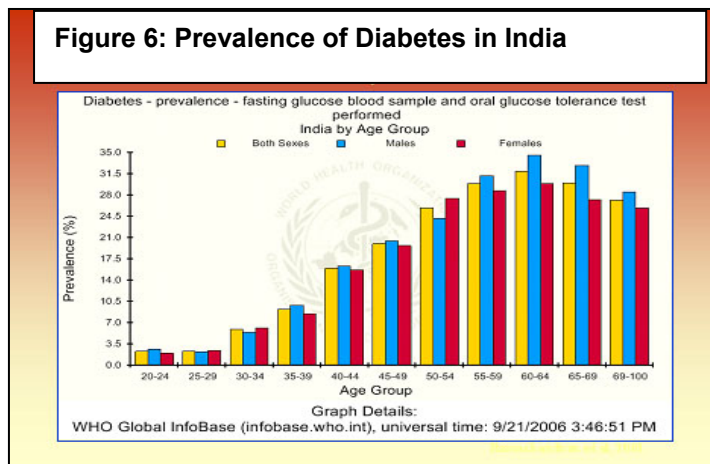
Such diets and lifestyles in India, while reducing under-nutrition, have exacerbated the incidence of obesity, (Figure 5)<sup>1</sup> abdominal obesity, insulin resistance, Type 2 diabetes and Syndrome X, as characterized by Dr. Gopalan. They have also resulted in a documented increase in other NCDs, including hypertension, coronary heart disease and cancer. Overall, India already faces an onslaught of both communicable diseases and chronic diseases, with the burden of chronic diseases already exceeding that of



communicable diseases. A survey of some 11,000 urban adults in South India in 2000 revealed that 35-45% of middle-aged urban adults have a body mass index (BMI) that exceeds 25.<sup>14</sup> Already by 1998, at least 20% of the men and 30% of the women in urban areas in India are considered to have abdominal obesity.<sup>15</sup> Dr. C. Gopalan projected that it would double between 2002 and 2010. In contrast, overweight prevalence in rural India remains low.

Meanwhile, physical activity and energy expenditure continue to decline as more and more of India's agricultural society evolves into industrialized communities. A WHO sub-national survey of over 10,000 urban and rural adults in India conducted in 2003 showed a high prevalence of physical inactivity, especially

## Type II diabetes



As with obesity, Type II diabetes among middle class adults and children in India is growing rapidly. Diabetes is now six to ten times more prevalent in India's urban populations than in rural populations, with prevalence among urbanites in the 40-60 age group estimated to range from 15-30%,

according to a survey in 2000 (Figure 6)<sup>14</sup>. The number of persons with Type II diabetes in India is expected to double from about 40 million currently to nearly 80 million by 2030. The death rate from cancer is also anticipated to increase from 700,000 in the year 2000 to over a million by the year 2020, and 5 million Indians a year are expected to die of cardiovascular disease by the same year. By that time, NCDs and injuries in India are expected to nearly double and account for 8 million deaths a year<sup>16</sup>.

### “Epidemic can be halted” prevention is the key

What can India do to reduce its risk of NCDs? Fortunately, chronic diseases are largely preventable, and there is strong scientific evidence that behaviour modification comprising a shift to healthful diets and a healthy lifestyle can largely prevent them, and that appreciable changes can occur rapidly.

In May 2004, WHO's World Health Assembly endorsed a Global Strategy for Diet and Physical Activity, outlining a comprehensive global health agenda and a policy framework for achieving behaviour change, the fundamental goal of which is risk reduction. The report underscores the importance of preventing chronic diseases, stating that treatment would place an intolerable economic burden especially on developing countries, where treatment of NCDs has to compete for resources with prevention of diseases of poverty<sup>17</sup>

In North America, Western Europe, Japan and Australasia, where NCDs have dominated the national health agenda for many years, active and sustained intervention in the diets and behaviours of populations has produced dramatic decreases in risk factors and premature death rates from heart disease and some tobacco-related cancers. This was achieved by cooperation among communities, governments, and food production and processing industries. In North Karelia, Finland, for example, age-adjusted cardiovascular mortality dropped dramatically between the 1970s and 1995, mostly because dietary change, combined with community action and consumer demand, resulted in lowered plasma cholesterol and blood pressure<sup>18, 5</sup>. South Korea has largely maintained its traditional high-vegetable, low-fat diet and achieved lower rates



of chronic diseases and obesity as compared to other industrialized countries. The national nutrition policy in India encompasses a multifaceted approach, including prevention of chronic diseases, but its overwhelming focus remains the prevention of childhood and maternal undernutrition and infectious diseases. India needs a philosophical and financial commitment towards tackling the growing challenge of NCDs, and should institute more public health policies and programmes directed towards their prevention.

### Focus on lifestyle modification and public education

Prevention entails lifestyle change, which, when considering the typical “affluent diet,” boils down to:

- eating green—a plant-based diet, high in vegetables, fruits and whole grains
- limiting energy intake from total fats and saturated fats
- limiting intake of free sugars and salt
- increasing physical activity to achieve energy balance and a healthy weight
- avoiding tobacco use
- limiting alcohol consumption.

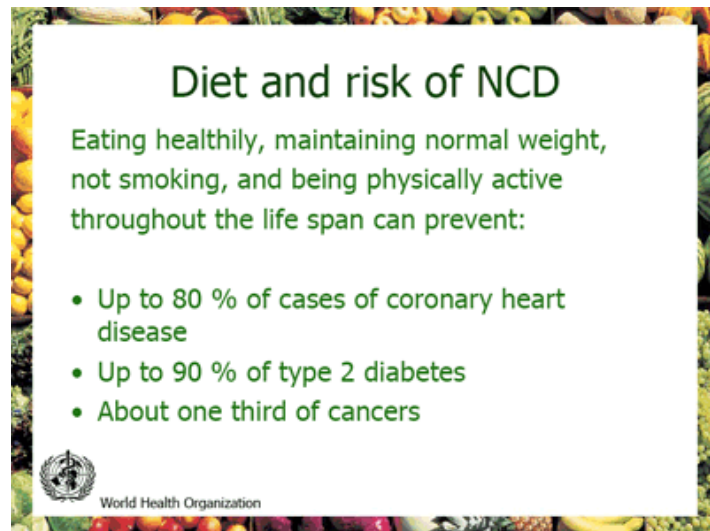
Of course, in India, under-nutrition must continue to receive attention. In the past three decades, similar recommendations have come from authoritative groups in different parts of the world, and they show a general consensus<sup>16, 19</sup>. In India, the Ministry of Health, NGOs, health professionals and educators are already focusing on NCDs, using many similar approaches. However, to promote public health, India needs to take advantage of a historic opportunity to reach and educate the masses through television and other mass media, which are India’s strength<sup>20</sup>.

Initiatives such as the Center for Communications, Health & the Environment’s (CECHE’s) Media Training Program in India in 1998<sup>21</sup> demonstrated the advantages of joint training for health and media professionals in health promotion and disease prevention (<http://www.ceche.org/communications/media1.htm>). Meanwhile, CECHE’s public health and nutrition scholarship program for Master’s degree and Doctoral candidates at Lady Irwin College in New Delhi<sup>22</sup> exemplifies the strong motivation among nutrition students for such training (<http://www.ceche.org/communications/lady-irwin/lady-irwin.html>).

Figure 7: Indian musicians sing praises of a healthy diet and lifestyle in a 20-minute program/song produced for TV by CECHE trainees



Almost all Indians now have access to radio and television. Since 1995, almost every village is believed to have at least one television set and communities often gather together to watch television. The visual media offer a special opportunity to inform and mould public opinion on nutrition and health issues. The paradox is that the Indian food



industry is using the same tools to push fast foods, and so far winning easily, because they have the resources and the know-how to attract people's attention. One way that the Ministry of Health, Doordarshan and the health sector could outsmart the industry and advertising agencies is to turn the tables on them by outsourcing PSAs, musicals, television series, and advertisements to the very advertising agencies that are producing for the industry. The advertisements could feature major celebrities such as Bollywood actors or sports heroes; lampoon bad eating habits and a "couch potato lifestyle", make it unattractive and costly in the long run to be obese, and bemoan lost years and quality of life, because an unhealthy diet means a high risk of getting sick, missing out on all the fun, not seeing grand children grow up, dying early, and so on.

Considering the impact the print media has had in promoting diet and lifestyle in industrialized countries like the United States, India could also use more "objective" means of publicity to compel the government and national lawmakers to develop policies and put programmes into action. In addition, it would be desirable for the country to review, and on at least some level, incorporate, such major global health-promotion campaigns as "5-A-Day The Color Way," which premiered in America and is now helping to encourage vegetable and fruit consumption across Europe through ads, PSAs and promotional materials targeting both children and adults<sup>23, 24</sup>.

### **Magnitude of risk reduction**

Experience in industrialized countries tells us that prevention of tobacco use alone could reduce the global disease burden by nearly 40 %. Consuming low-saturated fats and adopting plant-based diets, avoiding excess alcohol, and being physically active could cut disease risks by an additional 30 %, according to the National Academy of Sciences<sup>25, 26</sup>. In the case of specific chronic diseases, some experts estimate that lifestyle changes could yield up to an 80 % reduction in the risk of heart disease, a 90 % decrease in the risk of Type II diabetes, and ~30 % reduction in cancers<sup>27</sup>. The final test of how well mass media or other strategies work is whether NCD rates (e.g., obesity and the growing list of diseases it causes) go down. But interim measures are

essential for monitoring public awareness and changes in eating habits and lifestyles; to assess trends; to determine the impact of interventions; and to modify intervention techniques, if needed. In the 21st century, developing nations must not repeat the mistakes made by the Western world as it advanced. We have a historic opportunity to halt, or at least to minimize, the epidemic of chronic diseases in developing countries. The experience in industrialized countries tells us that this can and must be done.

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# **OUTREACH OF SAFE AND NUTRITIOUS FOOD: THE CHALLENGE STILL CONTINUES**

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## **Introduction**

The nutrition agenda in the earlier days was confined to 'protein'; the focus migrated slowly, with the expanding knowledge base, to 'protein calorie'; and today the nutrition problem encompasses all aspects of 'micronutrient' malnutrition. While the urban population is fairly aware of the various nutrition intervention programmes, the rural population does not have the access to nutrition knowledge that it urgently needs. In India both micro and macro nutrient deficiencies are widely prevalent in all sections of the population. It is important that all developing countries like India make an attempt to address these problems and evolve appropriate practical solutions, which can be implemented at the local level.

## **Science of food and nutrition**

I strongly believe that the concept of 'home food' has a very important role in outreach programmes, since it is the end-point in the chain of supply of semi-processed and processed foods. Other approaches, such as the introduction of innovative processed food products that are loaded with nutrition and yet manage to capture the cultural diversity of traditional foods, can make a difference. It is time we woke up and looked afresh at these possibilities for a paradigm shift and the way forward to solve nutritional problems in the country. Often there are problems in capacity development. Today there are many institutions such as national and international laboratories, universities and colleges in many of the developing countries, which offer training and courses in Food Science and Food Technology. If properly oriented, these young specialists would be a major force in spreading the nutrition message among the populations of these nations.

## **Role of innovative technologies in enhancing the nutritive value of cooking ingredients**

A large variety of ingredients are added during cooking, whether at the kitchen level or at the food processing level, at small, tiny, village, cottage, medium, large and global companies. Many a time, these ingredients add flavour and colour, enhance the taste, and give rheological properties and functional attributes to the food. They help in presenting the food in a form that is appealing to the consumer. The objective of adding any ingredient should be to enhance the quality of the food but, most importantly, any such added ingredient must be safe.

## **Nutraceuticals**

Ingredients added to the food during preparation generally do not add to the nutritional value. However, today we have another scenario with the advent of

nutraceuticals. These are becoming very important adjuncts in making processed foods healthy for the consumer. There are many ingredients with the label of “nutraceuticals” that go into food processing; the claims regarding their beneficial effects are sometimes valid and at other times exaggerated. It is imperative that all such claims are critically evaluated. Antioxidants, free radical scavengers, molecules claiming to improve the circulatory system, and a plethora of others already have a market of about US \$150 billion. It is claimed that many of these have synergistic effects with drugs on the one hand and with digestion of food on the other hand. Therefore the importance of ingredients cannot, at any point in time, be ignored in the chain of food processing; they form part of all processed foods, whether cooked in the home kitchen, a tiny, cottage, or village level industry, or in a multinational factory. Food processing prevents food wastage and can improve access to food at affordable cost. This is especially so when there is a concomitant increase in agricultural production and productivity. Sustainable agricultural production, along with robust village-level food processing programmes can go a long way towards improving rural livelihoods.

### **Nutrition: pediatrics to geriatrics – a food-based approach**

When we look at food processing, we need to worry about food safety and also cost effectiveness. I think it is here that nutrition plays a major role. When one looks at the fascinating life journey from the pediatric age to the geriatric age, one sees a number of “platforms” at which this journey pauses in an attempt to catch up with health and well-being, in the face of economic constraints which limit growth and even deny millions access to sufficient food. What then should be the role of doctors, nutritionists, scientists, policy makers and NGO’s involved in ultimately delivering health care at minimum cost? It is clear that food and nutrition play pivotal roles in this agenda of achieving health for the people throughout their life cycle.

### **Bioavailability of nutrients and nutrition – a policy outlook**

We look to food technology to bridge the gap between agriculture and outreach to the consumer. The focal point, both from the biotechnology point of view and from the processing point of view, is the enhancement of nutrient content through biotechnological approaches and retention of nutrients during processing and bioprocessing. There is a dire need today to address this issue and make efforts to improve the bioavailability of nutrients. For example, the bioavailability of iron can be improved by vitamin C-rich foodstuffs; for prevention of anaemia iron folic acid and vitamin B 12 are essential. We need to learn from our traditional foods, the synergy of formulations, which enhance the bioavailability of nutrients. These traditional practices have endured for thousands of years, based on the experiences of countless generations. We may do well to combine scientific insights with traditional wisdom to arrive at ideal food combinations to ensure bioavailability of nutrients.

### **Food safety**

Food safety is a major global issue today, especially because food moves across national frontiers. There is an urgent need to harmonise the food

safety regulations of various countries and the codex guidelines. It is often difficult to trust the information provided on food packaging labels. Whether it is a new high-technology product (such as artificially ripened bananas) or bottled or packaged water, or the additives in processed foods, or organic foods, or genetically modified foods, it is essential that the labelling should indicate the quality and safety aspects to the full satisfaction of the consumer. The problem of safety does not stem only from the small amount of contamination that may occur; the food moves through many points and undergoes many operations on its way from rural field to urban hypermarket. Typically, foods may have various contaminants, leading to varying levels of toxicity. Food safety calls for more than just detection of heavy metals, pathogens, chemical contaminants and residues. There may be other factors in certain foods that may produce allergic reactions or be incompatible with a specific section of the population or even certain individuals. This is where the role of nutrigenomics is important. It will be of great help in assuring food safety in the future. Food safety is a prerequisite for the long-term benefit of any food product. The claims and contents need to be clearly defined and understood, from farm to consumer.

The safety aspect of food has overtaken the issue of cost effectiveness in the consumer's outlook. Today's consumer gives more importance to safety, and is ready to pay more for an assured and guaranteed safe food product. But to deliver a safe food in commerce, with zero contamination of pesticides and heavy metals, and absence of toxins and pathogens, is not an easy task. It requires high levels of scientific and technological skills, and also the networking at different levels for effective implementation.

### **Public-private-partnership (PPP)**

Without firm and dependable food security, the nation's security itself can become shaky. Ensuring food security is not only the responsibility of the government. One must explore the possibilities of public private partnership (PPP) in building infrastructure, and also the potential for networking human resources. There is a need for a holistic approach towards ensuring food security in developing nations.

There is a role for technology in each link of the food chain, from field to factory to supermarket shelves. The amount of energy that goes through in the whole process: the amount of labour and skill that the farmer puts in, the amount of research and development that goes into increasing the productivity and safety of the food, and the highly sophisticated scientific and technological inputs that go into making a food product while retaining its inherent nutritive value and even enhancing it to deliver a healthy, safe and cost-effective food is team-work, contributing to different links in the entire chain. If there is one slip anywhere in the chain, the food becomes unsafe and unfit for human consumption. Therefore the entire chain has to be perfect. It is very important to realize that every step, from production in the field to disposal of the packaging material is important and vital.

It is agriculture that sustains the nation. Therefore agriculture requires top priority. Agriculture scientists, food technologists and nutrition scientists have to network and co-ordinate their efforts. They must ensure that the benefits of scientific advances are translated into more efficient agricultural practices, and more innovative food technology methodologies, so as to benefit society. It is an amazing team-work that we often do not recognize when we eat food three times a day, every day.

We have to think not only of undernourished people around the world who have only one meal every three days, but also, increasingly, of overnourished ones who represent the obesity problem. Changing circumstances demand that we change our approaches. To change is to risk something that makes us insecure. But not to change constitutes a bigger risk. We must change if we have to make a difference. Let us be confidently optimistic.



# DISCOVERY OF HUMAN ZINC DEFICIENCY AND IT'S IMPACT ON HUMAN HEALTH

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*It is truly a great honor for me to participate in this Festschrift honouring Dr. C. Gopalan. Dr Gopalan has contributed tremendously to the field of Nutrition. His contributions as Director of National Institute of Nutrition and as Founder President of Nutrition Foundation of India are indeed phenomenal and legendary. He has trained a large number of nutrition scientists in India and has played a very significant role in the field of nutrition globally. I met Dr Gopalan for the first time in 1988 when I was invited by the Nutrition Society of India to deliver the Gopalan oration and receive the gold medal. We have remained friends for the twenty years since then, and I have truly cherished this friendship. In this contribution honouring Dr. Gopalan, I will present the historical aspects of the discovery of zinc deficiency in humans and its subsequent impact on human health.*

## **Discovery of human zinc deficiency**

### ***Zinc deficiency in Iran***

I went to Shiraz, Iran, in June 1958 after finishing my formal training in medicine at the University of Minnesota Medical School, Minneapolis, Minnesota, USA. Dr Hobart A Reimann, formerly from the University of Minnesota, Department of Medicine, was the Chief of Medicine at the Nemazee Hospital of Pahlevi University in Shiraz, Iran. He invited me to join him to set up a curriculum for teaching medicine to students and house staff. In Shiraz, I met Dr James A Halsted, who was a Fulbright Professor at Pahlevi University and was primarily involved with Saadi hospital, an equivalent to City hospital in the USA. In the fall of 1958, I was invited by Dr Halsted to discuss a patient with anaemia at the medical centre grand rounds at the Saadi Hospital. The case was presented to me by Dr M Nadimi, Chief Resident, a graduate of the Shiraz Medical School.

The patient was a 21-year-old man who looked like a 10-year-old boy. In addition to severe growth retardation and anaemia he had hypogonadism, hepatosplenomegaly, rough and dry skin, mental lethargy, and geophagia. The patient ate only bread made from unleavened wheat flour and his intake of animal protein was negligible. He consumed nearly 0.5 kg of clay daily. The habit of geophagia (clay eating) was common in the villages around Shiraz. Further studies documented iron-deficiency anaemia in the patient. There was no evidence of blood loss. Inasmuch as 10 additional similar cases were brought to the hospital for my care within a short period of time, hypopituitarism as an explanation for the observed growth retardation and hypogonadism was discarded.

The anaemia in these patients responded to oral administration of iron. The probable factors responsible for anaemia in these patients were poor availability of iron in the diet, excessive sweating (thereby causing greater iron

loss from the skin than would occur in a temperate climate) and geophagia, which further decreases iron absorption. It was difficult to explain all of the clinical features solely on the grounds of tissue iron deficiency, inasmuch as growth retardation and testicular atrophy are not seen in iron-deficient experimental animals. The possibility that zinc deficiency may have been present was considered<sup>1</sup>. Zinc deficiency was known to cause growth retardation and testicular atrophy in animals. However, essentiality of zinc and its deficiency in humans was unknown. Because heavy metals may form insoluble complexes with phosphate, we speculated that some factors responsible for decreased availability of iron in these patients with geophagia may also have decreased the availability of zinc. O'Dell and Savage<sup>2</sup> first observed that phytate (inositol hexaphosphate), which is present in cereal grains, markedly impaired the absorption of zinc. We published a clinical description of the Iranian cases as a syndrome in 1961 and speculated that zinc deficiency may account for growth retardation and male hypogonadism in these subjects<sup>1</sup>.

### ***Zinc deficiency in Egypt***

I left Iran in January 1961. Subsequently I joined the department of Biochemistry and Medicine at Vanderbilt University, Nashville, Tennessee, under Dr. William J Darby. Although Dr. Darby wanted me to study porphyrin metabolism in pellagra in Egypt, I shared with him my speculation that zinc deficiency was prevalent in the Middle East and was responsible for widespread growth retardation. He was very interested in this idea. I then moved to Egypt and started my studies at the US Naval Medical Research Unit No.3 (NAMRU-3), Cairo. In Egypt, patients similar to the growth-retarded Iranian subjects were encountered. The clinical features were remarkably similar except that the Iranian patients had more pronounced hepatosplenomegaly, a history of geophagia, and no hookworm infection, whereas the Egyptian subjects had both schistosomiasis and hookworm infestations and no history of geophagia<sup>3</sup>. The dietary history of the Egyptian subjects was similar to that of the Iranians. The consumption of animal protein was negligible. Their diet consisted mainly of bread and beans (*Vicia fava*). Based on decreased zinc concentrations in plasma, red cells, and hair, and the studies with zinc- 65 that revealed, greater plasma zinc turnover, smaller 24-h exchangeable pool, and decreased excretion of zinc-65 in stool and urine in the dwarf patients as compared to the controls, we concluded that the dwarfs were zinc-deficient<sup>3</sup>.

Further studies in Egypt showed that the rate of growth was greater in patients who received supplemental zinc as compared to those receiving iron instead, or those receiving only an adequate animal-protein diet. Pubic hair appeared in all the subjects within 7-12 weeks after zinc supplementation. Genitalia increased to normal size and secondary sexual characteristics developed within 12-24 weeks in all the patients receiving zinc. In contrast, no such changes were observed in the iron-supplemented group or in the group on an animal-protein diet. Thus, we related the growth retardation and gonadal hypofunction in these subjects to zinc deficiency. The anaemia responded to oral iron treatment. These studies clearly showed that severe

anaemia and iron deficiency were not causative factors for growth retardation and hypogonadism in human subjects. Thus, our studies documented for the first time that zinc is essential for humans and that zinc deficiency is prevalent in the populations of developing countries.

### ***Zinc deficiency in other countries***

Clinical pictures similar to those reported in zinc-deficient dwarf patients from Iran and Egypt have been observed in many other countries. Cognitive impairment has also been observed in these patients. It is believed that zinc deficiency is present in countries wherein the population consumes primarily cereal proteins. A detailed study of zinc deficiency in geophagia cases from Turkey was reported by Cavdar *et al* in 1983<sup>2</sup>. Beneficial results of zinc supplementation on growth were observed. In 1974 a landmark decision to establish recommended dietary allowances (RDAs) for humans for zinc was made by the Food and Nutrition Board of the National Research Council of the USA National Academy of Sciences.

### ***Spectrum of clinical manifestations in zinc deficiency***

During the past four decades, a spectrum of clinical manifestations of deficiency of zinc in human subjects has emerged. On the one hand, the manifestations of zinc deficiency may be severe; and, at the other end of the spectrum, zinc deficiency may be mild or marginal<sup>4</sup>. A severe deficiency of zinc has been reported to occur in patients with acrodermatitis enteropathica (a genetic disorder), or after total parenteral nutrition (TPN) without zinc, excessive use of alcohol, or penicillamine therapy. The manifestations of severe zinc deficiency in humans include bulbous pustular dermatitis, alopecia, diarrhoea, emotional disorders, weight loss, intercurrent infections due to cell mediated immune dysfunctions, hypogonadism in males, neuro-sensory disorders, and problems with healing of ulcers. If this condition is unrecognized and untreated, it becomes fatal. The manifestations of a moderate deficiency of zinc include growth retardation and male hypogonadism in adolescents, rough skin, poor appetite, mental lethargy, delayed wound healing, cell-mediated immune dysfunctions, and abnormal neurosensory changes.

In our studies in the experimental human male model in whom only a mild deficiency of zinc was induced by dietary means, decreased serum testosterone level, oligospermia, decreased natural killer (NK) cell activity, decreased interleukin (IL)-2 activity of T helper cells, decreased thymulin activity, hyperammonaemia, hypogeusia, decreased dark adaptation, and decreased lean body mass were observed<sup>4, 5,6</sup>. It is, therefore, clear that a mild deficiency of zinc in humans affects clinical, biochemical, and immunological functions adversely.

### ***Impact of the discovery of human zinc deficiency***

When I first started my studies in the Middle East, I knew of only three enzymes, carbonic anhydrase, alcohol dehydrogenase and carboxy peptidase,

which required zinc for their activation. Today we know of over 300 enzymes that require zinc for their activation, and over 2000 transcription factors requiring zinc for their stability have been reported thus far<sup>4</sup>. Zinc is essential for cell-mediated immunity and its deficiency causes a Th1 to Th2 shift<sup>4</sup>. Zinc is also an antioxidant and anti-inflammatory agent<sup>4</sup>.

### **Therapeutic uses of zinc**

The therapeutic uses of zinc in humans are:

- treatment of acute infantile diarrhea
- treatment of acrodermatitis enteropathica
- treatment of wilson's disease
- treatment of sickle cell disease
- treatment of amd (age related macular degeneration)
- treatment of the common cold
- reduction in the incidence of infections in the elderly

### ***Acute infantile diarrhoea***

Acute infantile diarrhoea is a very serious disorder that affects millions of children in developing countries. The mortality rate associated with this condition is 60 to 80%. During the past decade, zinc in therapeutic doses has been used for treating such patients. This approach has reduced the mortality by 30 to 40%<sup>7</sup>. Also, it has been observed that the incidence of pneumonia drastically decreased in patients who received zinc<sup>8</sup>.

### ***Acrodermatitis enteropathica***

Acrodermatitis enteropathica is a relatively rare genetic disorder in which the absorption of dietary zinc is affected adversely such that the affected individuals become severely zinc deficient. If untreated, the disease becomes fatal. Mutation in the ZIP4 gene (a zinc transporter) is responsible for this disorder. Treatment with therapeutic levels of zinc is highly successful and nowadays such patients survive and lead normal lives<sup>4</sup>.

### ***Wilson's disease***

Wilson's disease is a genetic disorder in which copper accumulates in liver, kidneys, intestines, brain, and other organs. In our earlier studies we observed the beneficial effect of zinc on the sickling of deoxygenated sickle cells<sup>9</sup>. Later zinc administration in therapeutic doses (50 to 150 mg zinc daily given orally as acetate) was used for decreasing the pain crises in sickle cell disease patients. We observed that at this level of zinc administration, we were inducing copper deficiency in our patients<sup>9</sup>. This led us to evaluate zinc as a therapeutic modality for the treatment of Wilson's disease<sup>10</sup>. Zinc acts by induction of intestinal cell metallothionein in which, once induced, has a high affinity for copper and prevents the serosal transfer of copper into the blood. The intestinal cells turn over rapidly and take the complexed copper into the stool where it is excreted. Zinc blocks copper in the food and endogenously excreted copper

through salivary, gastric and other gastrointestinal juices. As a result, zinc produces a chronic negative copper balance<sup>10</sup>. For maintenance therapy of Wilson's disease, zinc is the treatment of choice. Zinc has no toxic effects and it can be used for treating pre-symptomatic patients and pregnant women.

### ***Sickle cell disease***

Our studies in adult patients with sickle cell disease showed that nearly two-thirds of these patients were zinc deficient<sup>11</sup>. We also related growth retardation, male hypogonadism and immune dysfunction in these patients to zinc deficiency<sup>11</sup>. Zinc supplementation in sickle cell disorder patients in therapeutic doses has shown beneficial effects in respect of the above-mentioned clinical parameters. Chronic haemolysis in these patients causes hyperzincuria, and this leads to deficiency of zinc.

### ***Macular degeneration***

The age-related Eye Disease Study<sup>12</sup> group supported by the National Eye Institute, NIH, conducted an 11-center double-masked clinical trial in patients with age-related macular degeneration (AMD). As many as 3640 participants were enrolled. Their ages ranged from 55-80 years and the average follow up period was 6.3 years. The participants were randomly assigned to receive daily oral tablets containing one of the following:

- antioxidants (vitamin C 500 mg, vitamin E 400 IU; and  $\beta$  carotene 15 mg);
- zinc 80 mg as zinc oxide and copper 2 mg as cupric oxide;
- antioxidants plus zinc; or placebo.

Copper was added in order to prevent copper deficiency in the zinc-supplemented group. The group taking the antioxidant-plus-zinc supplementation showed reduced risk of developing advanced AMD to the extent of ~25% and the risk of vision loss to the extent of ~19%. The group taking zinc alone showed a lower risk of developing advanced AMD to the extent of ~21% and vision loss to the extent of ~11%, whereas in the group taking the vitamins alone the risk levels for these conditions were reduced by ~17% and ~10%, respectively. No side effects were noted as a consequence of therapeutic levels of zinc supplementation. Another interesting observation was that only the zinc-supplemented group showed decreased mortality<sup>13</sup>. The effectiveness of zinc in AMD is most likely due to its antioxidant and anti-inflammatory effects.

### ***Zinc in common cold***

In order to test the efficiency of zinc acetate lozenges in reducing the duration of symptoms of the common cold, we carried out a randomized, double blind, placebo-controlled trial in 50 ambulatory volunteers recruited within 24 hours of developing symptoms of the common cold<sup>14</sup>. The participants each took one lozenge containing 12.8 mg zinc (as acetate) or placebo every 2 to 3 hours while they were awake, for as long as they had cold symptoms. Subjective symptom scores for sore throat, nasal discharge, nasal congestion, sneezing,

cough, scratchy throat, hoarseness, muscle ache, fever and headache were recorded daily for 12 days<sup>14, 15</sup>. When compared with the placebo group, the zinc group had shorter mean overall durations of cold symptoms, cough and nasal discharge, and lower total severity scores for all symptoms<sup>14,15</sup>. The mechanism by which zinc may mediate the common cold is not well understood. It has been suggested that zinc may act as an antiviral agent. Another possibility is that extra-cellular zinc ions may exert their antiviral effect by stabilizing and protecting cell membranes. Zinc is known to induce production of interferon and modulate inflammatory cytokines, which in turn may result in alleviating the symptoms of the common cold.

Our recent studies in the elderly have shown that the incidence of infection, oxidative stress bio-markers and generation of inflammatory cytokines, were significantly lower in subjects who received supplements of 45 mg zinc (as gluconate) daily than in the placebo groups<sup>16</sup>. This study demonstrates the effect of zinc, *in vivo*, on immune functions, and its role as an antioxidant and anti-inflammatory agent. We have observed similar effects of zinc supplementation in patients with sickle cell disease<sup>17</sup>.

## Conclusion

Deficiency of zinc and its essentiality for humans was recognized nearly 45 years ago. Major manifestations of zinc deficiency include growth retardation, hypogonadism in males, immune dysfunction and cognitive impairment. Significant advances have taken place in understanding the biochemistry of zinc. Zinc is essential for the functioning of immune cells. It is estimated that nearly 2 billion subjects in the developing countries may have zinc deficiency. The therapeutic impact of zinc is also very impressive. Zinc therapy in infantile diarrhoea, Wilson's disease, acrodermatitis enteropathica, sickle cell disease, and the common cold, and zinc supplementation for prevention of blindness in age-related macular degeneration and for the prevention of infections in elderly subjects and in patients with sickle cell disease are some of the major uses of zinc supplementation in humans.

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## **EFFECT OF EARLY CHILDHOOD UNDERNUTRITION ON REPRODUCTIVE PERFORMANCE: A LONG TERM FOLLOW UP STUDY**

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*When I first met Dr. Gopalan, he was Director-General of the Indian Council of Medical Research. At that time I was working in the ICMR headquarters, New Delhi, and was part of the central coordinating team for the ICMR collaborative study on short-term sequelae of induced abortion. During the ICMR scientific meetings I used to enjoy Dr. Gopalan's incisive concise comments and clear, quick decisions. I never thought he even knew of my existence, and so I was surprised when, a few months later, he sent for me. He told me that after discussions with Dr. Srikantia, the then Director of National Institute of Nutrition (NIN), he had decided that I should look after the clinical component of the WHO-ICMR collaborative study on the effects of hormonal contraceptives in undernourished women, being carried out at NIN Hyderabad. I told Dr. Gopalan that I had earlier participated in ICMR clinical trials on hormonal contraceptives and knew how to conduct them, but all I knew about nutrition was what was taught to undergraduates in medical college and most of it may not be applicable to undernourished women; and so I was not sure whether I was the right person for the task. Dr Gopalan explained that what NIN needed was a person with experience in clinical trials with hormonal contraceptives; they would help me with the nutritional aspects initially; I would have to work hard and acquire the necessary nutritional knowledge as fast as I could and complete the trial successfully. I was still not sure, but Dr. Srikantia smiled and nodded his head, and my journey in the uncharted seas of nutrition began.*

*NIN is a very hospitable institution; between learning and working, my initial few months at NIN flew. Beginning with Dr. Bamji, who was looking after the laboratory component of the study that brought me to NIN, I have many life-long friends among my colleagues and NIN has remained my home. At the end of one year, I knew that the study was going well. The hospital OPDs where we were recruiting cases also catered to pregnant and lactating women, and soon I was also studying IM iron therapy for moderate anemia in pregnancy, and lactation–nutrition–fertility interactions.*

*When I met Dr. Gopalan about a year later, he was happy with the progress of the study. He then mentioned that Dr. Sathyanarayana at NIN was studying the effect of early childhood undernutrition in adolescent boys, and that it was time to initiate a study in adolescent girls in the same cohort, to assess the impact of early childhood undernutrition on their reproductive performance. I was taken aback and said I had never carried out community-based studies; the answer was, it was high time for me to learn! It was the beginning of my lifelong association with community-based interventions to improve health and nutritional status within the existing primary health care infrastructure.*

*The study on 'the effect of childhood nutritional status on reproductive performance' was completed two years later; by then both Dr Gopalan and Dr*



*Srikantia had retired. Even today I regret that, discouraged by the statements that the findings were along the expected lines and so not worth publishing, I did not send the data from this study for publication. I am writing a brief review of this study, as my tribute to Dr. Gopalan who created a legion of nutrition scientists by using his uncanny ability to spot the potential in persons and then pushing them into challenging tasks to hasten their professional development.*

*A decade in NIN was followed by a decade on the Division of Epidemiology and Communicable Diseases at ICMR headquarters and nine years as Adviser (Health and Nutrition), Planning Commission. The day after my retirement, I joined Nutrition Foundation of India – completing a full circle.*

## **Introduction**

Chronic undernutrition from early childhood continuing through adolescence into adult life is common among poorer segments of the population. There had been speculations about the adverse effects of undernutrition in childhood on reproductive performance. However, in the seventies, there had been very few studies investigating this aspect. The major problem in mounting such a longitudinal study in which follow-up for about two decades is essential, was that it is unethical to follow-up and not intervene if the children had health or nutrition problems. On the other hand, if the children were to receive appropriate intervention during this period and benefit from it, the group might not suffer from any of the consequences that may have occurred in the absence of such intervention.

During the late seventies, NIN had the unique opportunity of undertaking a study 'the effect of childhood nutritional status on reproductive performance'. Nearly two decades earlier, in twenty-six villages near Hyderabad, children had been enrolled at birth and a nutritional survey of all children under five years of age had been carried out for five consecutive years. These children were part of a large cohort in whom prevalence of vitamin A deficiency was investigated. All the children belonged to an essentially homogenous rural population group in whom environmental and health care interventions were minimal. None of the children received any major nutritional or health intervention during the study. After a lapse of seven years their growth status during adolescence was evaluated.

In these villages, teenage marriages and conceptions were the rule. There were 912 girls belonging to the cohort who were traceable. An attempt was made to follow up these girls to obtain information on:

- age at menarche
- age at marriage
- age at first conception
- nutrition status during pregnancy
- course and outcome of pregnancy
- lactation performance and
- survival and growth of the offspring.

The relationships between childhood nutritional status, current nutrition status and reproductive performance were explored<sup>1</sup>.

### **Age at menarche**

There was a gradient in the mean age at menarche in the group; the girls who had been well nourished in childhood continued to be better nourished as adolescents and attained menarche earlier. The girls, who had been undernourished as children, were shorter and weighed less, as compared to those who were well nourished in childhood. The age at menarche was delayed in girls who had suffered from severe undernutrition during childhood. Because of this delay, the severely undernourished girls were able to make up early deficits in height observed through childhood and early adolescence. However they continued to weigh less than their better-nourished counterparts.

### **Age at marriage**

Girls who were normally nourished or showed mild undernutrition during childhood got married at an earlier age than those who were moderately and severely undernourished during childhood. This might partly be attributable to the fact that, in rural India, menarche is often followed by marriage within the next few months. Most of the normally nourished girls came from economically better off families; this might also have been partly responsible for their getting married at an earlier age.

### **Course and outcome of pregnancy**

A majority of these girls conceived within a year of marriage. They were followed up at least once during the first, second and third trimesters of pregnancy. Data on changes in anthropometric indices of nutritional status, haemoglobin levels, and course and outcome of pregnancy were collected. There was a significant difference in mean height between the normally nourished and severely undernourished girls; nearly six percent of the severely undernourished girls had a height of less than 140cm, which is known to be a risk factor associated with low birth weight and higher perinatal mortality rates (Table 1). Girls who were normally nourished in childhood had body weights comparable to those of the rural low-income group population throughout their pregnancies. Girls who had experienced varying grades of undernutrition during childhood weighed less. The proportion of girls with body weight less than 40 kg was higher among those who had suffered moderate and severe undernutrition during childhood. In spite of differences between the pre-pregnancy weights of normally nourished and undernourished girls, there were no significant differences in weight gain during pregnancy between these two groups. Nor were there any differences in the mean haemoglobin levels and prevalence of moderate to severe anemia between girls belonging to different grades of nutritional status during childhood.

Group (according to childhood nutritional status)	Height (cm)	% with less than 140 cm	Wt (kg)	% less than 40 kg	Arm circumference (cm)	Skinfold thickness (mm)	Hb (g/dl)	% with Hb <8.0 g/dl
Severely undernourished	148.6±1.02* (25)	5.9	46.3±1.04 (27)	35.3	20.3±0.44 (27)	9.5±0.55 (27)	9.4±0.36 (20)	11.8
Moderately undernourished	151.5±0.78 (44)	-	46.3±0.79 (37)	40.0	21.5±0.26 (37)	9.7±0.41 (35)	9.5±0.32 (17)	11.1
Mildly undernourished	150.9±0.78 (38)	1.6	47.2±0.87 (45)	18.0	21.5±0.26 (45)	10.6±0.50 (45)	9.7±0.29 (28)	4.9
Normal	155.7±0.99 (25)	-	50.2±1.12 (25)	6.7	21.9±0.33 (24)	10.0±0.75 (12)	9.3±0.39 (15)	10.0

Values are mean ± S.E.; Figures in parentheses indicate number of women, p< 0.05 as compared to normal; Source: Reference 1

An analysis of the data relating to course and outcome of pregnancy showed that there were no significant differences in the course and outcome of pregnancy between the groups, except for a marginally lower foetal loss rate in normally nourished girls. The mean birth weight of the infants, except those of the severely undernourished girls, was comparable to those born to primipara in rural low-income groups. The mean birth weight was lower and the proportion of infants weighing less than 2.5kg at birth was significantly higher among infants born to girls who were severely undernourished during childhood (Table 2). This could be partly due to the lower maternal weight during pregnancy and partly to coexisting adverse socio-economic and environmental factors. The observed higher infant deaths among infants born to severely undernourished girls might be partly due to the higher proportion of infants born with low birth weight, and adverse environmental factors in these households.

Group (according to nutritional status in childhood)	Foetal loss %	Birth weight (kg)	Birth weight below 2.5 kg (%)	Death during infancy %
Severely undernourished (37)	11.8	2.41± 0.090	52.9	11.8
Moderately undernourished (49)	8.9	2.57± 0.065	42.2	8.9
Mildly undernourished (66)	8.2	2.55± 0.057	37.1	3.3
Normal (30)	3.3	2.62± 0.089	38.3	6.9

Values are mean ± S.E; Figures in parentheses indicates numbers  
Source: Reference 1

### Lactation performance

Lactation was successfully initiated in all these rural girls without any difficulty. All the girls followed the traditional pattern of unsupplemented lactation for periods up to six months. There were no differences in the pattern of introduction of supplementary feeding to breast-fed infants. There were no significant differences in the mean body weight of the infants during the first

six months of age, among infants born to girls who had suffered from various grades of undernutrition during their childhood.

### **Summary and conclusions**

This long-term follow-up study showed that the delay in age at menarche in girls who had suffered severe undernutrition during childhood is perhaps one of Nature's compensatory mechanisms to improve adult heights; this delay also protected these girls from too early marriage and conception. In the late 1970s and early 1980s, the reproductive performance of this cohort was comparable to that of the rural women from these villages.

The villages in which these studies were conducted are no longer typical villages. They have become part of the periurban complex around the rapidly growing city of Hyderabad. Socioeconomic and life-style transitions in these erstwhile villages have been very rapid. There were no follow-up studies of these mothers-child dyads in the intervening 25 years. Now these children are in their late twenties, and their mothers are in their forties. Maybe the time has come for NIN to take up studies to assess the current health and nutritional status and assess how these mother-child dyads have fared.

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# PUBLIC INVESTMENT IN INFRASTRUCTURE DEVELOPMENT, AND ITS EFFECT ON POVERTY REDUCTION AND NUTRITIONAL IMPROVEMENT

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## Introduction

Poverty is quite widespread in India. Poverty, undernutrition and malnutrition are closely associated. Government interventions of nutritional supplementation (both calories and micronutrients) are in operation, but these cannot offer a permanent solution for the prevailing nutritional problems in the population, especially in rural communities. Eradication of poverty is a long-term solution that will enable the rural community to improve their nutritional status. The Government is undertaking programmes of infrastructure development for poverty reduction in rural areas through R & D, road development, education, improvement in health services, etc. An analysis of these inputs shows that road development has the maximal impact on poverty reduction, followed by education, health services, etc. But it is not known to what extent nutrition improves even in those who rise above the poverty line. It is desirable that organizations like NNMB, which survey the nutritional status of rural communities, should also collect socio-economic and other outcomes of Government investment and relate the poverty (income) of families/individuals to their nutritional status.

## Prevalence of poverty

Poverty is the cause of the low standards of living that are commonly seen both in rural and urban areas, but more so in rural areas. Poverty is recognized as the reason for inadequate dietary intake; however, malnutrition continues to exist among the non-poor, while adequate nutrition is not impossible, even in the diets of the poor<sup>1</sup>. The poverty line, as described in India, is Rs. 49 worth of expenditure per month at 1973/74 prices<sup>2</sup>. It is also defined as Rs 15 of income per capita per month at 1960-61 prices<sup>3</sup>. In the early decades of the Twentieth Century, the incidence of rural poverty was recognized to be quite high; it has declined over the decades from about 65 % prior to the mid-1960s to about 33% by the early 1990s (Table1). This steady reduction in poverty was strongly associated with agricultural growth in India, particularly the green revolution<sup>2</sup>, which in turn was in response to massive investments in rural infrastructure.

Year	% of Population below the poverty line Planning Commission i.e. 2200 kcal/day )			World Bank estimate (1992)
	Rural	Urban	Combined	
1972-73	54.1	41.2	51.5	55
1977-78	51.2	38.2	48.3	51
1983-84	40.4	28.1	37.4	45
1987-88	27.5	20.1	29.9	39
1993-94	21.0	14.0	19.0	37

Programmes	Target-Groups	Nutrients supplied
Supplementary feeding Programme	Preschool children Pregnant women	75g supply food. 300 Kcal/d; 125g suppl. Food 500 Kcal/d
Vitamin A prophylaxis programme	Preschool children	20,000 iu synthetic vitamin A (retinol) every 6 months orally
Anaemic – prophylaxis programme	Pregnant women preschool children	Iron (60mg) – folate (500 µg)/d per adult and half of it for preschool child.
National Goitre Control programme	All population universal	Iodized edible salt with 30ppm iodine
Midday meal programme	School children 6-10 years	Serve mid-day meal providing Kcal and protein.

Public intervention to combat malnutrition and undernutrition has been in operation since 1971, with the supply of food material and nutrients to vulnerable people directly through social or health services of the Government (Table 2). These intervention strategies were conceived, developed and tested at the National Institute of Nutrition, Hyderabad. Dr. Gopalan, as Director of the Institute at that time, played a leading role in these efforts. Some of the intervention strategies that were developed under Dr Gopalan's guidance were:

- iron-folate tablet distribution to pregnant woman, lactating women and preschool children to prevent iron deficiency anaemia (IDA)
- massive-dose vitamin A administration periodically to preschool children to prevent vitamin A deficiency and nutritional blindness, and
- supplementary feeding programmes to overcome energy deficiency among preschool children, and pregnant and lactating women. Besides the above three programmes, iodized salt distribution is under operation since 1960, to combat goitre. Currently, the midday meal programme is also in operation to improve the nutritional status of school children of 6-10 years of age in government-run schools.

Prior to the 1970s, protein deficiency was considered to be a major nutritional deficiency problem among preschool children in developing countries. This conclusion was drawn on the basis of clinical studies of the cases of kwashiorkor and marasmus that were prevalent among young children (1-3 years of age) belonging to the poorer socio-economic groups in several developing countries. However, systematic dietary and growth studies were carried out among preschool children in the rural areas of India by the ICMR<sup>4</sup>. A detailed analysis of the results by Narasinga Rao *et al* indicated that the primary deficiency among these children was not protein deficiency but energy deficiency, and that protein deficiency was only secondary to energy deficiency (food deficiency). These results were seconded strongly by Dr. Gopalan, and subsequently these were accepted by other nutritionists all over the world. Since then, the treatment of undernourished preschool children has been based on supplementary feeding of cereal-based foods, providing about 300 kcal of energy and 10g of protein.

Nutrient	Preschool children		NPNL women	
	Mean intake per day	As % of RDA	Mean intake per day	As % of RDA
Energy (Kcal)	807.0	65	2106.0	73 <sup>b</sup>
Protein (g)	20.9	91	53.8	108
Fat (g)	12.9	37	29.7	100
Calcium (mg)	239	48	509	127
Iron (mg)	7.7	64 <sup>b</sup>	19.7	63 <sup>b</sup>
Retinol (µg)	133	33 <sup>c</sup>	295	49 <sup>c</sup>
Thiamine (mg)	0.3	50	1.2	114
Riboflavin(mg)	0.4	57	0.9	72
Niacin(mg)	5.0	62.5	13.0	94
Ascorbic acid(mg)	15.0	38 <sup>c</sup>	40.0	100
Folic Acid (µg)	57.5	-	-	-
Zinc (mg)	4.3	54 <sup>c</sup>	154.9	

<sup>a</sup>National Nutrition Monitoring Bureau Report (1996-97); RDA: Recommend Dietary Allowances for Indians (1990); b. Macronutrients affecting Hb levels c. micronutrients affecting Hb levels

The governmental intervention to prevent and correct the deficiencies of energy, vitamin A, and iron are only transient measures that may correct the deficiencies among some of the children, but cannot permanently eradicate these deficiencies from the community at large. Further, the above-mentioned deficiencies represent only the severest cases of malnutrition among the vulnerable, poorer segments of the community; mostly in rural areas. These vulnerable preschool children, and pregnant and lactating women, have several other nutritional deficiencies such as those of calcium, B vitamins, particularly riboflavin, folate and vitamin B<sub>12</sub> (Table 3), with levels of dietary intakes well below RDA levels, with the associated health consequences. It must also be recognized that the correction of severe deficiency of any single micronutrient cannot be fully achieved without correcting all the concomitant deficiencies of other micronutrients. For example, it is reported that iron deficiency anaemia cannot be fully corrected with supplementation of iron tablets unless other co-existing deficiencies such as those of vitamin A, riboflavin, zinc, and pyridoxine, apart from folate and B<sub>12</sub>, are also fully corrected<sup>6</sup>.

Energy deficiency and deficiencies of several micronutrients (undernutrition) are more prevalent among the poor, but they are also to be found in those who are above the poverty line. Nutrition education to the very poor, urging them to improve their diets to correct the existing deficiencies of nutrients, will be ineffective given their financial constraints, but in those above the poverty line education may help to improve their diets, thereby correcting the nutrient deficiency. Therefore the primary aim of government intervention should be to eradicate poverty, that is, raise the poor populations above the poverty line as a first step, if the current programmes of intervention with energy (food) and micronutrients, along with appropriate educational messages, are to bear dividends.

**Table 4: Effect of Government Expenditure on poverty productivity**

Expenditure Variable	Marginal impact of spending 1.00 billion TFP	Number of Poor reduced/ Rs. Million
R&D	6.98	91.4
Irrigation	0.56	7.4
Roads	3.03	165.0 <sup>x</sup>
Education	0.43	31.7 <sup>x</sup>
Power	0.02	2.9
Soil and Water	0	6.7 <sup>x</sup>
Rural Development	NA	27.8 <sup>x</sup>
Health	NA	4.0

TFP: Total factor productivity; NA: not available; x: Significant at the 5 percent level

The primary goal of allocating public funding as efficiently as possible is to achieve an effective and early reduction in rural poverty to coincide with improved nutrition. The present goals conceived by the World Bank and other agencies<sup>7</sup> are for reducing the prevailing poverty in developing countries, predominantly in Asia, Africa and Latin America, by 50% by the year 2015. It is to be seen what impact reduction of poverty will have on the

nutrition of such populations that are raised above the poverty line. Public spending is generally directed towards agriculture and development (R&D), education, irrigation, road construction, power, soils and water, rural development and health services (Table 4). The effect of every additional unit spent under each of these heads on the number of poor reduced has been worked out. Earlier, when the effect of spending under possible heads was computed using a single equation, it was not possible to bring out the full effect, since there are multiple effects of spending on each of these items. Multiple simultaneous equations have been used to bring out the effect of spending 1 million rupees on poverty reduction. These results are given in Table 4. Every additional outgo of 1 million on road construction, results in the highest reduction in the numbers of poor people (i.e. 165/million). The prevalence of rural poverty would be reduced by 0.9 percent if the government were to increase investment in rural roads by 100 billion (1993 constant price). This phenomenon of higher effect on poverty reduction because of investment in rural roads has also been observed in other developing countries like China<sup>8</sup> and Vietnam<sup>9</sup>.

Investment in roads reduces rural poverty through growth in agricultural productivity, and also increases nonagricultural employment opportunities, at higher wages. Increased productivity accounts for 24% of the total impact on poverty reduction, nonagricultural employment accounts for 55 %, and increase in rural wages accounts for the remaining 31 %. Of the total productivity effect on poverty, 75% arises from the direct effect of roads in increasing rural incomes while the remaining 25% is from lower prices of agricultural inputs (15 %) and increased wages (10 %). Government investment in agricultural research and development (R & D) has the second-largest effect on mitigating rural poverty. One million spent on R & D would raise 91 poor people above the poverty line, although this expenditure is not directly targeted to the poor. If R & D were to be deliberately targeted to the poor, it might have a much greater impact on poverty reduction<sup>10</sup>.

Government spending on education has the third-largest impact on rural poverty reduction. An additional 1 million rupees spent on education would



raise 32 poor people above the poverty line. Most of this effect would arise from greater non-farm employment opportunities and increased wages. Education as a simple ratio has only a modest impact on agricultural TFP (Total Factor Productivity) Growth. Tornqvist Sheil Index, defined as aggregate output less aggregate inputs). Government expenditure on rural development has the fourth-largest impact on poverty reduction. Every extra 1 million of expenditure would raise 28 poor people above the poverty line. Government expenditure on irrigation has the fifth-largest impact on poverty reduction. Every extra 1 million would raise 7 poor people above the poverty line. Public irrigation impacts poverty through its impact on productivity. Its impact is enhanced by its catalytic role in stimulating private investment in irrigation. Government expenditures on soil and water conservation and health have only a small impact on rural poverty, and the impact is statistically insignificant. Total factor production (TFP) for 100 billion is highest with R & D (6.98); next come road construction (3.03), irrigation (0.56), and education (0.43), in that order.

### **Investment and returns in terms of poverty reduction and development levels in the rural areas**

Until recently, infrastructure (such as roads) construction in a rural area was not perceived as an important means of reducing poverty. Infrastructure has multiple links to poverty reduction as highlighted in the World Bank's Annual Report of 2001<sup>11</sup>. Improved infrastructure helps create jobs and raise the productivity of workers. It saves time and human effort in transporting water, crops, wood and other commodities. It also improves health (by reducing indoor air pollution in urban areas and making clean water available) and education (by expanding access to schools, computers and lighting). Among all types of rural infrastructure, rural transport is the most crucial for the livelihood of the rural poor. Improving the facility to reach schools promotes school attendance. In India, road construction in rural areas has been shown to reduce poverty. In the past, the Government of India's investment was biased towards irrigated and rain-fed areas. But studies have shown that road building favours poverty reduction in low-potential low-rain-fed areas to a larger extent than in rain-fed or high-potential areas.

While planning for infrastructure, viz. roads, the government should select poorer regions. This would be a win-win for growth along with poverty reduction. For example, in terms of poverty reduction, every additional kilometer of road would lift 1.57 poor people out of poverty in an irrigated area, but would lift 3.5 and 9.51 people out of poverty in high-potential and low-potential rain-fed areas, respectively. International Food Policy Research Institute (IFPRI), Washington, used state-level data from 1970 to 1993 to compute the impact of development programmes on poverty. The results show (Table 5) that additional government spending on roads is found to have the largest impact on poverty reduction, with agricultural extension and development having the second-largest impact.

## Investment in Agriculture

Agriculture is the largest sector of spending in many developing countries. Of the world's poor, most live in rural areas and are primarily engaged in agriculture. Therefore expenditure on agriculture is one of the most important governmental instruments for promoting economic growth and alleviating poverty in rural areas in

Investment	No. of poor Reduced per Million Rupees spent	Return in Rupees per Rupee spending
Roads	123.8(1)	5.31(2)
Agriculture R&D	84.5(2)	13.45(1)
Education	41.0(3)	1.39(3)
Health	25.5(4)	0.84(7)
Soil & Water conservation	22.6(5)	0.96(6)
Anti poverty programmes	17.8(6)	1.09(5)
Irrigation	9.7 (7)	1.36(4)
Power	3.8(8)	0.26(8)

Source: Fan, Hazell and Thorat 2000 Poverty line is defined as Rs 15 per capita per month at 1960-61<sup>2</sup>

developing countries. Although R & D is the largest component of government spending, it is observed in India that spending on roads makes the largest impact on reducing poverty per million rupees spent as compared to other classes of spending such as education, health, and soil and water conservation. These results are based on state level analyses and are given in Table 5. All these expenditures have a major effect, i.e.  $123.8 + 84.5 + 41.0 + 25.5 + 22.6 = 298.4$  persons are removed from the poverty pool for every million that is spent. Other spending like those on anti-poverty programmes, irrigation and power will reduce the numbers of the poor only  $17.8 + 9.7 + 3.8 = 31.3$  for every million spent under each of these categories.

## Poverty of individuals and their nutritional status

It was pointed out earlier that poverty is associated with undernutrition and malnutrition. The close association between the economic status (poverty) of a family and its nutritional status needs to be clearly established. In other words, which is the lowest economic status that can be associated with minimal nutrient intake sufficient to ensure normal nutritional status? Not only the number of poor persons raised above the poverty line, but also how high above the line a poor family has to be raised before it can afford a low-cost

CED Grade	BMI	1975-79 Survey		1989-90 Survey		1996-97 survey	
		Male	Female	Male	Female	Male	Female
Obese	≥25	2.3	3.4	2.6	4.1	3.8	6.0
Normal	18.5-25	42.1	44.8	48.4	46.6	50.5	46.6
CED grade 1	17.0-18.5	29.5	25.9	27.7	25.1	25.9	23.2
CED grade 2	16.0-17.0	14.7	13.2	12.5	12.9	11.0	12.8
T CED Grade3	<16	11.4	12.7	8.8	11.3	8.6	11.8
Total CED	≤18.5	55.6	51.8	49.0	49.3	45.5	48.2

balanced diet to provide all the nutrients at the minimal RDA levels, have to be identified. It is reported<sup>12</sup> that, even though poverty may be reduced by 50%, malnutrition may not be reduced by the same extent. For example, according to the Planning Commission, poverty during 2000 in terms of energy intake stands reduced to 25% of the population (Table 1). But according to the NNMB Survey<sup>13</sup> undernutrition (BMI status) (<18.5) has been shown to be 40-50% (Table 6) while prevalence of low weight for age in children below 5 yrs (from NNMB data) is shown in Table 7.

Age (years)	Sex	Weight for Age			
		>=90% Normal	75-90% Mild	60-75% Moderate	< 60% Severe
1-3	Boys	10.0	37.6	44.8	7.6
	Girls	9.3	40.1	42.0	8.6
	Pooled	9.7	38.9	43.3	8.1
3-5	Boys	7.6	43.5	44.7	4.2
	Girls	8.9	41.0	45.1	5.0
	Pooled	8.3	42.3	44.8	4.0
1-5	Boys	8.3	40.6	44.8	5.8
	Girls	9.1	40.6	43.6	6.7
	pooled	8.9	40.6	44.3	6.2
6-9	Boys	5.1	31.7	55.4	7.8
	Girls	5.9	31.0	54.1	9.0
	Pooled	5.5	31.4	54.7	8.4
10-13	Boys	2.5	14.8	55.1	27.5
	Girls	2.8	18.2	49.2	29.9
	Pooled	2.7	16.6	52.0	28.8
14-17	Boys	2.1	15.8	53.8	28.3
	Girls	3.8	34.6	51.6	10.0
	Pooled	3.0	25.5	52.7	18.9

NNMB survey 1996-97<sup>13</sup>

Data on prevalence of undernutrition in under four children is shown in Table 8. There are substantial differences in the prevalence of undernutrition between states.

- The association between poverty level and nutritious diets (below and above poverty line) can be established by community diet and nutrition surveys by NNMB and economic surveys by organizations like the National Sample Survey Organisation. Besides diet and nutrition surveys, additional economic status of the family (monthly income) to establish the poverty status of the family.
- Government spending on different categories like
  - agricultural R &D
  - roads
  - education
  - rural development, soil & water conservation irrigation etc., in the village surveyed can be collected information like any normal standard of living with at least a normal intake of energy and other nutrients close to RDA levels may be recorded.

The level of earning should be recorded, for which the lowest-cost balanced diet, providing minimal required level of nutrients as given in Table 9, becomes affordable by the family. Families whose diets meet the minimum energy requirements are above the poverty line according to the Planning Commission, but not according to other definitions of the poverty line. It will also be necessary to define the earning or expenditure class, which is able to afford the recommended levels of energy and other nutrients as per the latest RDA. A monthly income of Rs 49 at 1973-74 prices is defined as poverty line. This has to be translated to income at the current period (period of the survey) and the nutrient intake and nutritional status at this level of income have to be determined. From these data, it is then necessary to define the minimum level of income associated with RDA levels of nutrient intake.

State	Weight for age	Height for age
	Percentage below -2SD	
Delhi	41.6	43.2
Haryana	37.9	46.7
Himachal Pradesh	47.0	-
Jammu-Kashmir	44.5	40.8
Punjab	45.9	40.0
Madhya Pradesh	57.4	-
Uttar Pradesh	59.0	59.5
Bihar	62.6	60.9
Orissa	53.3	48.2
West Bengal	56.8	-
Assam	50.4	52.2
Gujarat	50.1	48.2
Maharashtra	54.2	48.5
Andhra Pradesh	49.1	-
Karnataka	54.3	47.6
Kerala	28.5	27.4
Tamil Nadu	48.2	-
All India <sup>x</sup>	53.4	52.0
National Family Health Survey 1992-93		
14		

Low cost balanced diet (sedentary man)	g/day	Content of Nutrients	
		Nutrient/day	Quantity/day
Foods g/day		Calories (kcal)	2738.60
Cereals	460	Protein (g)	66.60
Pulses	40	Calcium (mg)	781.60
Leafy vegetables	50	Iron (mg)	62.20
Other vegetables	60	Vitamin A(µg)	715.00
Roots & tubers	50	Riboflavin (mg)	1.15
Milk	150	Thiamin (mg)	2.45
Fats & Oils	40	Vitamin C (mg)	74.80
Sugar & Jaggery	30	Niacin(mg)	15.66
		Total fat(g)	66.90

It is desirable for NNMB to change the strategy of its survey programmes so as to link the nutritional observations with socio-economic data and the impact of various government programmes in reducing the poverty level. If this is done, the nutritional observations can be

linked to the level of poverty, the monthly income can be linked to government investments such as R&D, roads, communication, education, rural development, irrigation etc., (vide Table 5). This approach will also help in identifying families with a certain level of income who can be targeted for appropriate nutrition education in order to help them to improve their diets to ensure intake of all the nutrients at the RDA levels.

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# INFANT FEEDING AND OBESITY

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## Introduction

The association between adult obesity and increased risk of chronic diseases like diabetes and cardiovascular diseases is well known. The observed rapid escalation of overweight and obesity in the past two decades is therefore a cause for great concern. The rising prevalence of childhood obesity is receiving greater attention because of its association with adult obesity and its complications. Increasing consumption of energy-dense diets and reduced physical activity are recognized as major contributing factors. Recent studies suggest that nutritional practices in early life can also influence subsequent obesity, which has now become the focus of interest. This paper reviews the studies on early life risk factors, including birth weight, infant feeding and growth.

## Prevalence of childhood obesity

An increasing prevalence of obesity is reported in children and adults in both industrialised and developing countries. Data from National Health and Nutrition surveys in US showed that the prevalence of overweight in children (6-19 yr) was 15.4 % in 1999-2000, as compared to 10.9 % in 1988-94<sup>1</sup>. Similar trends are seen in developing countries that are undergoing rapid economic and epidemiological transition<sup>2</sup>. For example, in Brazil, a fast-growing developing country, the prevalence of overweight and obesity in children (6-14 yr) more than tripled (from 4.1% to 13.9%) between 1975 and 1997. In China, the prevalence of overweight in children of similar age increased from 7.7 % to 12.4 % within a 6-year period (1991-1997). The prevalence rates are higher in urban than in rural populations. Reports from India also indicate a high prevalence of obesity among the affluent urban populations<sup>3-5</sup>. In Punjab, ~10 % of adolescent children (10-15yr) belonging to affluent families were found to be overweight, and 5-6 % were obese<sup>3</sup>. A recent survey of affluent school children in Delhi showed that 22 % were overweight and 6 % were obese<sup>4</sup>.

The rising prevalence of childhood obesity is of great concern because of its association with adult-onset diseases. Long-term studies show that childhood obesity affects adult morbidity and mortality<sup>6</sup>. Approximately 50% of adolescents with BMI above the 95th percentile become obese adults. Furthermore, the rates of cardiovascular disease and diabetes also increase, and a higher mortality risk from all causes especially cardiovascular disease was demonstrated in men who had been obese during their adolescence. Obesity prevention has now become a global public health priority, but preventive strategies focused on adults or those in their late childhood years have largely been unsuccessful. The focus has now shifted to early-life risk factors, including birth weight, infant feeding and growth.

## Birth weight, child growth and adult health

There is mounting evidence that events occurring early in life, even before

birth, can influence health and disease in adulthood later. Maternal nutrition is an important determinant of birth weight, and there is evidence that birth weight can influence child growth and long-term health. A higher maternal BMI in pregnancy is associated with higher birth weight, more rapid growth during childhood, and an increased risk of obesity in adult life<sup>7</sup>. Low birth weight (LBW) is associated with central obesity in adulthood, which confers increased cardiovascular risk<sup>8</sup>. Epidemiological studies by Barker showed an inverse relationship between LBW and coronary heart disease (CHD) decades later<sup>9</sup>. Subsequent studies have shown that LBW also increases the risk of insulin resistance and diabetes<sup>10,11</sup>. Barker's group also examined the effect of postnatal growth on disease risk<sup>12</sup>. They surveyed >8000 persons in Finland, whose childhood growth had been carefully recorded. A total of 444 subjects were admitted to hospital with CHD or died of the disease. These individuals had had a relatively small body size in the first two years of life, and grew more rapidly from 2-11 years. This pattern of small body size at birth, low weight gain in infancy and adiposity rebound in childhood was also associated with type 2 diabetes in adult life<sup>13</sup>. Studies in adolescent children showed similar results. LBW and high BMI during childhood were associated with impaired glucose tolerance in Indian children<sup>14</sup> and hypertension in Jamaican adolescents<sup>15</sup>. These findings indicate that interventions to improve foetal growth and to control obesity in childhood are likely to be important factors in the prevention of chronic diseases in later life.

### **Infant growth and childhood obesity**

One issue that remains unresolved is the role of early postnatal growth in the first two years of life. In contrast to Barker's observations, other studies on full term and premature infants suggest that rapid growth during infancy can result in subsequent obesity. Stettler *et al.* reported a multi-centre study wherein complete data were available for over 19,000 children from birth to 7 yr<sup>16</sup>. The prevalence of overweight at 7 yr was 5.4%. They found that rapid weight gain during the first 4 months of life was associated with increased risk of overweight status at 7 yr. This association was independent of birth weight and remained significant even after adjustment for several confounding factors.

Baird and colleagues conducted a systematic review of studies on both size and growth in infancy in relation to later obesity<sup>17</sup>. This included 22 cohort and 2 case control studies. Of these, 18 assessed the relationship between infant size and subsequent obesity, most of them showing that infants who were obese, and who were at the highest end of the distribution for weight or BMI were at increased risk of obesity. Ten studies assessed the relation between infant growth and subsequent obesity, and most showed that infants who grew more rapidly were at increased risk of obesity in later life.

### **Childhood BMI and adult obesity**

There are several studies showing that childhood obesity is associated with increased risk of adult obesity. Whitaker *et al.* investigated the association in over 800 young adults born in Washington State, USA, between 1965 and

1971<sup>18</sup>; 16% of them were over weight, with BMI > 85th percentile. The probability of obesity in adulthood was higher among those who were obese during childhood. After adjustment for parental obesity, the odds ratio for the association ranged from 1.3 for obesity at 1- 2 yrs of age to 17.5 for obesity at 15-17 yrs. Thus, the study showed that childhood obesity is an important predictor of adult obesity, regardless of whether the parents are obese.

A Swedish study examined the association between rapid weight gain in early childhood and body composition at the age of 17 yr<sup>19</sup>. It was a prospective cohort study in 248 children. The results showed that increasing weight gain during infancy and early childhood were both independently associated with larger BMI, fat mass and fat-free mass at 17 yr. Thus, rapid weight gain in infancy and in childhood is a risk factor for later adiposity. It is hypothesized that these are different processes and may allow separate opportunities for early intervention against obesity in later life.

Eriksson *et al.* tracked obesity from early life into adulthood in a birth cohort of approximately 4500 people in Finland<sup>7</sup>. The cumulative incidence of obesity in adults was 33.8%. The incidence increased with increasing body size at birth. Adult obesity was associated with significantly higher weight and BMI at all ages from 6 months to 12 yr. Childhood BMI was a stronger predictor of adult obesity as compared to body size at birth.

### **Infant feeding and early growth**

Since early growth is related to feeding pattern, the relationship between infant feeding and obesity has become the focus of interest. WHO recommends exclusive breastfeeding for the first 6 months but many infants are fed commercial infant formula during this period, and follow up studies show that their growth pattern is different from that in breastfed infants. For example, in a longitudinal study of American infants, weight for length was similar in the first two months, but thereafter breastfed infants grew less rapidly as compared to formula-fed infants<sup>20</sup>. There were significant differences in skin fold thickness and percent body fat in later infancy, indicating that breastfed infants were leaner than formula-fed infants even in populations of high socioeconomic status. Several studies have confirmed these growth patterns and led to the development of new WHO growth charts taking the breastfed infant as the normative growth model<sup>21</sup>.

The observed differences in growth patterns of infants may be related to the feeding behaviour, with self regulation of intake being inherent in breastfeeding as against fixed amounts in bottle feeding. Mothers who breastfeed their infants are more responsive to infants' needs, while formula feeding is highly controlled, with the mother deciding when and how much the child should consume. Mothers who bottle-feed their infants are anxious to see that the bottle is finished, and this often results in overfeeding. Studies measuring the milk intake have shown that the milk volume per feed, as well as total milk consumption in a day, is higher in formula-fed than in breastfed infants<sup>22</sup>. Consequently, energy and protein intakes are also higher, accounting for more rapid weight gain in formula-fed infants. The age at which



solid foods are introduced can also influence nutritional intakes and growth rates. Whitehead *et al.* found that bottle-fed infants were introduced to solid foods sooner than were breastfed infants<sup>23</sup>.

### **Infant feeding and childhood obesity**

Growth studies show that weight gain is slower in breastfed infants than in formula-fed ones. There is also evidence that growth rate during infancy can influence subsequent weight gain and BMI. This has led to the hypothesis that breastfeeding protects against obesity, while formula feeding may increase the risk. This raises the question of whether the effect is clinically relevant, and if so what measures can be taken to offer protection for non-breastfed infants.

In recent years, several studies have been published with conflicting data on the relationship between breastfeeding and childhood obesity. Some studies show a protective effect while others find no effect. For example, Bergmann *et al.* examined 480 children from a longitudinal birth cohort who were breastfed or formula-fed<sup>24</sup>. By 3 months, formula-fed infants showed higher BMIs and thicker skin folds than breastfed infants did. Significant differences were seen from 6 months onwards. In formula-fed infants, the prevalence of obesity nearly doubled, and then tripled from the age of 4 yr to 6 yr. Thus the study shows that early formula feeding brings on the obesity rebound in early childhood, predictive of obesity in later life. On the other hand, Zive *et al.* found no association between infant feeding and childhood obesity in 4-yr-old American children<sup>25</sup>. BMIs and skin fold thickness were not related to any of the infant feeding variables, namely, duration of breast feeding, formula feeding, or the age at which complementary foods were introduced. The main limitation of these studies is the small sample size.

Subsequent studies included large numbers of children. For example, Armstrong *et al.* conducted a population-based study in a cohort of approximately 32,000 Scottish children<sup>26</sup>. A health check at 3-4 yr of age showed a significantly lower prevalence of obesity among breastfed infants even after adjusting for confounding effects of socioeconomic status and birth weight. These results suggest that breastfeeding reduces obesity risk in childhood. Von Kries conducted a cross-sectional survey of >9000 German children aged 5-6 yr at the time of entering school<sup>27</sup>. Their weights were analyzed in relation to data relating to feeding in early life, as obtained from their mothers. Results showed that the prevalence of obesity in children who had been exclusively formula-fed was 4.5% as compared to 2.8% in exclusively breastfed children. There was a clear dose-response effect of breastfeeding. Prevalence of obesity decreased with increasing duration of breastfeeding. Thus the study suggests that prolonged breastfeeding can reduce the risk of obesity in later life.

Other studies have shown variable results. Grummer *et al.* examined the link between breastfeeding in the first 2 yr of life and weight status at 4 yr of age, using data from the Pediatric Nutrition Surveillance System, covering over 170,000 children<sup>28</sup>. They found a dose-response relationship between breastfeeding and the risk of overweight only among non-Hispanic whites; but

there was no such significant association in Blacks or Hispanics. Hediger *et al.* examined data from the National Health and Nutrition Survey of children at 3-5 yr<sup>29</sup>. The sample included diverse ethnic groups, as in the earlier study. Although breastfeeding appeared to protect against obesity, there was no statistically significant association with duration of breastfeeding. In a longitudinal analysis of an Australian cohort, infants breastfed for 12 months were found to be leaner at that age, but no differences were found at 8 yr of age<sup>30</sup>. Wadsworth *et al.* suggest that the observed association between breastfeeding and obesity may be accounted for by social factors associated with breast feeding<sup>31</sup>.

The effect of breastfeeding can be modified by early dietary factors. For example, a recent study showed that exclusive breastfeeding for 4 months had a protective effect against obesity risk at 7 yr among children who had consistently low fat intake at 12, 18 and 24 months<sup>32</sup>. This effect was not seen in those with high fat intake in the second year of life. In another study, higher intake of animal protein at 12 months and 5 yr was positively associated with higher body fat percentage at 7 yr<sup>33</sup>. These results indicate that dietary intakes during childhood are as important as breastfeeding during infancy for preventing obesity.

### **Infant feeding and adolescent obesity**

In most of the earlier studies, children were examined up to 6-8 yrs. Others examined obesity in adolescent groups. Gillman *et al.* analyzed a cohort of approximately 15,000 young adolescents aged 9-14 yr, who were children of women who participated in the Nurses Health Study<sup>34</sup>. About 85% of them had been breastfed for at least 6 months. After analyzing for a number of confounding factors, they found that infants who were exclusively or mostly breastfed for 6 months had significantly lower risk of obesity than children who were breastfed for a shorter period of 3 months. A school-based study in the Czech Republic found that breastfeeding was associated with a 20% reduction in the risk of obesity up to the age of 14 yr<sup>35</sup>. Similar observations were made by Tuldahl *et al.*, who measured body composition with dual energy X-rays<sup>36</sup>. Children who were exclusively breastfed for more than 3 months were leaner than non-breastfed infants. However, others found no consistent relationship between breastfeeding and adolescent measurements<sup>37,38</sup>. Although breastfed infants tended to be shorter and leaner, the effect was markedly reduced or no longer significant after adjusting for confounding factors.

There are several reasons for the inconsistent results. These include retrospective collection of data, inadequate control of confounding factors, differences in sample size, short duration of breastfeeding and inadequate information on infant feeding practices. For example, both breastfed and non-breastfed infants received additional forms of nutrition, such as cow's milk or cereal, and the timing of introduction of these foods was not clearly delineated. Furthermore, data were collected over a 40-year time span during which there substantial changes in infant formulas and environmental factors had taken place. These limitations compromise the interpretation of studies relating to the effects of breastfeeding versus formula feeding.

Notwithstanding these limitations, systematic reviews and meta-analysis of published studies suggest that breastfeeding has a small but consistent protective effect against obesity risk in childhood<sup>39-41</sup>. On the basis of 11 studies, Dewey concluded that breastfeeding reduces the risk of childhood obesity to a moderate extent<sup>39</sup>. There is an inverse relationship between breastfeeding duration and childhood obesity. An analysis of 9 studies by Arenz<sup>40</sup> and 17 studies by Harder<sup>41</sup> confirmed the dose-response association.

The evidence for the protective effect of breastfeeding against obesity comes almost entirely from observational studies, which have a potential for confounding and selection bias. Recently, Kramer *et al.* assessed the effect of breastfeeding in the Promotion of Breastfeeding Intervention Trial (PROBIT), which is a cluster-randomized trial of a breastfeeding promotion intervention based on the WHO/UNICEF Baby-Friendly Hospital Initiative<sup>42</sup>. Nearly 14,000 infants enrolled at Belarussian maternity hospitals were followed up to the age of 6 yr. The intervention led to a much greater prevalence of exclusive breastfeeding at 3 months in the experimental group than in the control group (43.3% as compared to 6.4%) and a higher prevalence of any breastfeeding throughout infancy. But no significant effects of the intervention were observed on height, BMI, skin fold thickness or blood pressure. These results are consistent with those of the recently published meta-analysis conducted by Owen, and they suggest that previously reported beneficial effects on these outcomes may be the result of uncontrolled confounding and selection bias<sup>43</sup>.

### **Infant feeding and adult obesity**

Promotion of breastfeeding has been suggested as a strategy for reducing obesity in adult populations. Although overweight children tend to become obese adults, few studies have directly addressed the relation between infant feeding and adult body weight. In a recent study, Michels *et al.* investigated the association in approximately 36,000 participants in the Nurses Health Study II. The participants were followed prospectively from 1989-2001<sup>44</sup>. Mothers of participants provided information on the duration of breast- and bottle-feeding, and information on body weight at ages 5, 10 and 18 yr, and the current weight was reported by the participants. The results showed that the duration of breastfeeding was not related to being overweight or obese during adult life. Women who had been exclusively breastfed as infants for more than 6 months had a risk of 0.94 of becoming obese as adults, as compared to those who had not been breastfed as infants. Exclusive breastfeeding for more than 6 months was associated with leaner body shape at age 5 yr as compared to those who were not breastfed, but this association did not persist during adolescence or adulthood. Thus the study shows that breastfeeding is unlikely to play an important role in controlling the obesity epidemic.

### **Summary**

There are numerous studies suggesting that breastfeeding offers a protective effect against obesity in childhood. Promotion of breastfeeding has been suggested as a strategy for reducing obesity. Although overweight children

tend to become obese adults, few studies have directly addressed the relationship between infant feeding and adult body weight, and the results of research are variable. This may be due to retrospective collection of data, inadequate information on feeding practices and inadequate control of confounding factors. An alternative explanation may be that infant feeding and weaning practices exert a relatively greater influence on adiposity in early childhood, but that thereafter, genetic and environmental factors play a larger role in determining obesity. These include dietary habits and physical activity, which are known to influence BMI and body composition throughout life. Regardless of its role in preventing obesity, breastfeeding has many advantages for the mother and child, and its continued promotion and support remains a public health priority. However, promotion of breastfeeding is unlikely to have much impact on the current obesity epidemic, unless additional measures are taken to promote healthy diets and active life styles.

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## **NUTRITIONAL REQUIREMENT OF THE AGED**

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In the year 2006/07 the Nutrition Foundation of India conducted a Symposium on “Nutrition in early childhood”. No doubt it is extremely important to take all possible steps to provide proper nutrition to children so that they grow up to be healthy and useful citizen of India. This of course does not mean that there is no need for concern for the quality of nutrition for those who are in their very advanced age, somewhat infirm and subject to various age related disabilities.

Government of India’s National Policy of Older persons announced by the Ministry of Social Justice and Empowerment in 1999 clearly recognised the importance of nutrition for a healthy old age. The relevant extract from the policy is quoted below:

“Older persons and their families will be given to educational material on nutritional needs in old age. Information will be made available on the foods to avoid and the right foods to eat. Diets and recipes suiting tastes of different regions which are nutritious, tasty, fit into the dietary pattern of the family and the community, are affordable and can be prepared from locally available vegetables, cereals and fruits, will be disseminated.”

The life span is increasing rapidly due to medical advances and it is estimated that in India the number of those above age 75 will grow to about 25 million by 2011. People born today will live beyond 100 years. It is inevitable that with growing age, the natural immune system of the body weakens, and many ages related disabilities such as lack of mobility, impaired cognition, memory loss, poor eye sight and lack of hearing etc. begin to appear.

If we examine the institutional care facilities available for older persons in the country today, we will understand the extent of our un-preparedness as a society to deal with the challenges that the population ageing is going to pose on our resources, both, human and material. Therefore, it is not only desirable but also essential that we devise ways and means to ensure that we don’t just add years to life, but add life to years of these older persons so that they remain healthy and independent. For this nutrition is the first imperative.

Proper nutrition is a basic requirement at all stages of life but it is important to differentiate between the nutritional requirements at various age levels. The food and nutritional requirements for infants, growing children, young upto the age of say 50, the old, and the very old are possibly quite different from each other. As the very old i.e. over 75 may not be physically very active, their energy requirements may be quite low; but their other macro and micronutrient requirements continue to be high; nutritious food is necessary for maintenance of good health. Nutrition Foundation of India being an important organization in field of nutrition research should clearly specify optimal food and nutrient requirements essential for maintenance of good health in older persons.

# AYURVEDIC CONCEPTS OF NUTRITION AND DIETARY GUIDELINES FOR PROMOTING /PRESERVING HEALTH AND LONGEVITY

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*I have great pleasure in dedicating this article to Dr. C. Gopalan, the outstanding nutritionist from India, on his 90<sup>th</sup> birth anniversary. In a span of over three decades of a distinguished career as the architect of the prestigious National Institute of Nutrition (NIN), at Hyderabad, and later as the Director-General, Indian Council of Medical Research, he contributed significantly to the progress of medical science/research in the country. Subsequently, in the past 25 years, almost single handedly, Dr. Gopalan has founded, nourished and steered the Nutrition Foundation of India (NFI). Thanks to his dynamic leadership and vision, today NFI stands tall as a voluntary body of international stature in the field of nutrition science policies, advocacy and nutrition education, apart from ably fulfilling its major role of bridging the gap between nutrition knowledge and its application (through research, analysis, community education and advocacy). Dr. Gopalan is a role model for future generations, as one who has successfully fulfilled the real purpose of human life (the 'purushartha'), through a life-time of hard work and the single-minded devotion of a "Karmayogi", in his chosen field of Nutrition Science - a cause he was 'called' to serve nearly sixty years ago!*

## Introduction

The ancient Indian System of Medicine literally means "The Science of Life (or Living)", which actually represents a way of life that incorporates the art of healing through harmony with Nature and the environment (comprising all the living forms existing on planet Earth). The approach of Ayurveda to life and living is holistic and its range cosmic, while its application is universal and far-reaching, because it is based on certain eternal facts/principles that have not changed with time. As a system of medicine, Ayurveda dates back approximately three to four thousand years. It is considered as an Upa-veda (or branch of the original Vedic sciences<sup>1, 2,3</sup> particularly Rigveda and Atharva veda. True to its holistic approach, Ayurveda addresses the preventive as well as the curative aspects of medicine. Its definition of health is so comprehensive that it outdoes the WHO definition, by incorporating the physical / physiological, psychological, social as also the spiritual aspects of human life. Thus, Sushruta<sup>4</sup> (600 B.C) defines a healthy person as one in whom there is perfect balance of all bodily functions with tranquility or equilibrium of the mind senses and spirit (or soul). Clearly demarcating the preventive and curative aspects of Medicine (as a discipline), Charaka (700 B.C) states: "Medicine is of two kinds: One is promotive of vigour in the healthy, and the other, destructive of diseases in the ailing"<sup>5</sup>.

Modern researches and health care authorities (and unfortunately, a majority of Ayurvedic physicians too) in India tend to focus their attention mainly on the curative aspects, particularly in trying to find or offer "less expensive" and



“less harmful” alternative remedies from the vast *materia medica* of Ayurveda. These efforts miss out on the original message of wisdom from Ayurveda, pertaining to the “wellness” or preventive aspect. Guidelines offered in Ayurveda for preserving one’s health (throughout the life span) are not only scientific, but practical and entirely workable (with a “common sense” approach) at the levels of individuals, community, society and in clinical practice. They are also highly relevant today, when Mankind (in all parts of the world) is exposed to and suffering from the ravages of highly “artificial life styles” adopted by individuals and societies/communities, consequent to modern civilization, urbanisation and technology explosion, apart from severe competition and stress in daily life.

Ayurveda gives elaborate guidelines for achieving perfect health and remaining healthy in its “Swastha Vritta” (literally meaning “on being healthy”) through Dinacharya (daily routine) and Ritucharya (seasonal regimens). Comprehensive instructions are given on specific food/dietary schedules (for different times of the day, different seasons, according to one’s age and most importantly, to suit one’s individual constitution or “Prakriti”). Apart from nutrition, measures for *personal hygiene*, use of *medicated gargles*, *oil massages* and *regulated physical exercises* (based on the Yoga system) are prescribed. Further, Ayurveda advocates<sup>6</sup> that individuals should not suppress natural physical (physiological) urges like micturition, defecation, sneezing, yawning, as also hunger, thirst, sleep, tears etc. (and to properly regulate the ‘sexual’ urge). On the other hand, Ayurveda advocates suppression of harmful psychological urges (ie. negative emotions) like anger, fear, greed, vanity, jealousy, malice, as also excessive attachment (to anything). Importance is given to maintaining mental health by cultivating a positive attitude and Sadvritta (adherence to a strict code of moral principles and conduct, throughout life), apart from measures of relaxation such as meditation, prayer, group activities etc. It is interesting to note that, today, renowned cardiologists, neurologists and psychiatrists from the developed countries are advocating the same principles for modifying lifestyles so as to prevent/manage dreaded diseases such as heart attacks, stroke, stress disorders, cancers, diseases of ageing, etc. through non-drug measures, as supplements to medications and surgery that are routinely being practised in the modern era.

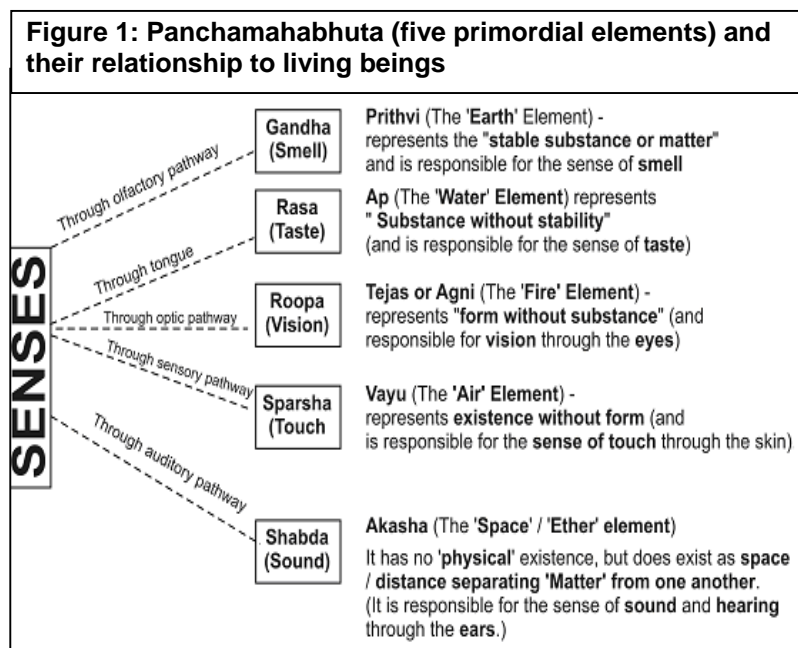
Apart from “Swastha Vritta”, Ayurveda offers another unique principle/therapy or technique - “Rasāyana tantra” for preventing or countering the adverse effects of ageing. The Rasāyana drugs/ measures of Ayurveda encompass the whole gamut of anti-ageing, anti-oxidant, adaptogenic/anti-stress, immunity-conferring food items, drugs and other measures (like meditation, achāra rasāyana or behavioural code for positive health). ‘New Age Ayurveda’ (from Western countries) had added many new plant drugs to the list of Ayurvedic Rasāyanas (such as ginkgo biloba, ginseng, evening primrose oil, etc.)<sup>7</sup>.

The ultimate goal of Ayurveda- (the Science of living) is to help Mankind to live a healthy, long life, mainly to achieve the well recognised four-fold purpose of human life viz. the chaturvidha purushārtha (encompassing

specific targets in life). To our ancients, human birth and life did not represent an accidental phenomenon (or a passive event to be completed mechanically), but a meaningful journey (from birth to death) for each individual with definite, time-tested goals to be achieved in consecutive stages of life (from childhood and adulthood to old age- terminating in death). This four-fold purpose of human life comprises: dharma (learning righteousness and moral values to be practised throughout life, especially in carrying out one's duties with moral responsibility); artha (acquisition, by just means, of material wealth); kāma (fulfilling one's desires and well deserved enjoyment of the pleasures of life, within the frame work of dharma – with respect to social and family life, particularly in adulthood and middle age), and finally moksha (salvation or liberation of the 'soul' through spiritual pursuits, in old age). To attain this four-fold purpose of life, Ayurveda considers it essential, for a human being to maintain oneself not only in a disease-free condition, but also in a state of perfect, positive health, balancing the body, mind and spirit <sup>8</sup>.

Ayurveda considers each human being as a distinct individual born with unique physiological/metabolic characteristics (most of which remain constant throughout life). These distinct characteristics, which contribute to the physical, physiological (metabolic) and psychological make-up of each individual, are described under the term Prakriti in Ayurveda. As Ayurveda believes in maintaining harmony with the internal as well as the external milieu, it is important to determine the "Prakriti" of each human being for maintaining health and preventing diseases, by following certain specific schedules relating to life-style, (including dietary guidelines) for each prakriti. In this article, the physiological/metabolic part of prakriti is mainly dealt with. For details on 'mental parameters' of prakriti, one may refer to David Frawley<sup>9</sup> and Partap Chauhan.<sup>10</sup>

To understand the concept of 'prakriti', however, it is essential to first get familiar with some of the fundamental principles of Ayurveda<sup>11, 13</sup> such as the pancha mahabhūtas (the five primordial elements); the tridoshas (Vata, Pitta and Kapha), the Sapta dhatus (the seven primordial/basic bodily tissues), and the trigunas, apart from the basics of Ayurvedic pharmacology (rasa, guna, veerya, vipaka, karma, prabhava of all substances – including food items and drugs). The "pancha mahabhūtas" (the five primordial elements) are considered the building blocks of all physical matter that exist on our planet (organic and inorganic; animate and inanimate;



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the living and the non-living). These five elements are the Prithvi (the earth element), Ap (the water element), Tejas or Agni (the fire element), Vayu (the air element) and Akasha (the space or ether element). The pancha mahabhūtas are the origin of the physico-chemical basis of all matter. For a proper grasp of the “five element theory”, it is important to desist from interpreting the elements on the basis of a literal translation of the Sanskrit terms, but to take them as symbolizing a unique, subtle analogy to explain the ‘material’ component of the planet, as we perceive it. As depicted in (Figure 1 & Table 1), each of these elements (while constituting the building blocks of all physical matter), also serves vital functions in the living organism, by being associated with a specific sense organ (and its proper functioning throughout life).

<b>Table 1: The fundamental principles of ayurveda</b>
The pancha mahabhutas (the five primordial elements), The building blocks of nature / universe (both organic & inorganic; animate / inanimate; living / non-living) Prithvi (earth), ap (water), tejas (fire), vayu (air), akasha (space/ether)
The “tridoshas”(vata, pitta & kapha) All psychobiological functions of the human body are carried out and experienced by the actions and attributes of these three “doshas”.
➤ The sapta dhatus (seven primary tissues) These are the primary / basic building blocks / units of the human body (with specific functions) rasa, rakta, mamsa ,medas, asthi, majja and shukra / Arthava
Agni and ama Agni (not to be confused with Tejas or Agni bhuta / element) is a unique concept of Ayurveda accounting exclusively for the complex enzymatic / biochemical processes involved in digestion & metabolism, as also absorption, assimilation and transformation into and development of dhatus. Three major types of Agni described in the body are: <ul style="list-style-type: none"> <li>➤ jatharagni (responsible for digestion and metabolism in the gastro-intestinal tract)</li> <li>➤ seven dhatwagnis (responsible for tissue metabolism in each dhatu)</li> <li>➤ bhutagni (agni in each primordial element or bhutas, assisting in processing of all ‘matter’, according to situation). Incomplete / defective processing by agni, at any level, gives rise to ama (partially digested or metabolized product), leading to various disease conditions.</li> </ul>
† *For details, see fig. 2 <i>From Gross to subtle; from prithvi (earth) to akasha (space)</i>

## The “Tridoshas”

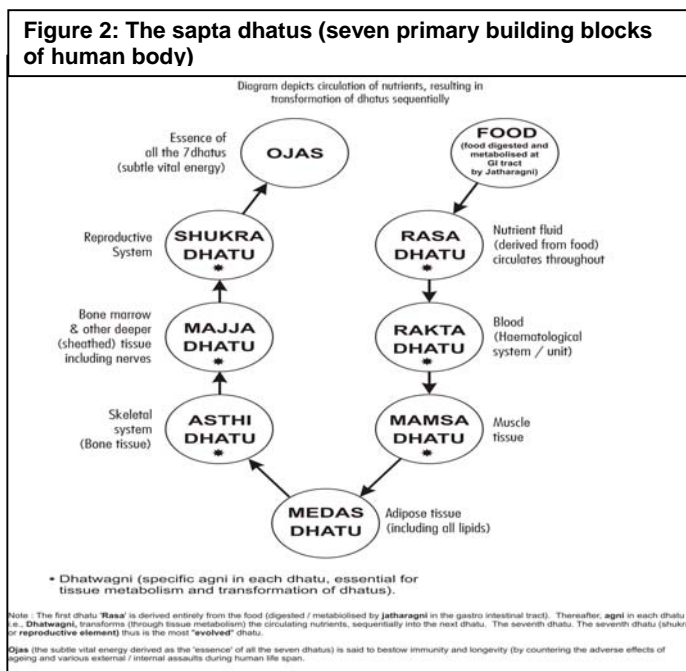
The three ‘doshas’ (Vata, Pitta, Kapha), in Ayurveda, account for all the psycho-biological functions of living beings. They are called “doshas” (ie. “defective “or “vitiated” elements), because they are functional elements which are unstable and highly vulnerable to vitiation, although paradoxically, they need to exist and function in a state of ‘balance’ or ‘equilibrium’ to maintain perfect health (and prevent disease conditions). The three ‘doshas’ are more functional (rather than structural or anatomical) units; they still comprise the five primordial elements. Thus, vata, the most unstable of the doshas is composed of the air (vayu) and space/ether (akasha) elements, pitta is composed of fire (tejas) and water (ap) elements, whereas kapha, the most stable of the three doshas is composed of earth (prithvi) and water (ap) elements. Each of the doshas has its own properties and functions in the human body (Table 2).

	VATA	PITTA	KAPHA
Elemental constitution	Air (Vayu) + Space (Akāsha)	Fire (Tejas) + Water (Ap)	Earth (Prithvi) + Water (Ap)
Physical Physiological Attributes	Mobility, Breathing, Natural Urges, All sensory & motor functions; secretions, excretions.	Heat generation (mobile energy), Hunger, Thirst, Digestion and Metabolism, Vision;	Lubrication, Body building, stability (static energy) Immunity
Psychological (mental) attributes	Restlessness Anxiety Fear	Intelligence Anger, hate, Malice	Patience / forgiveness Attachment / hoarding (possessiveness)

- All major neurological functions / activities (including CNS), locomotion, respiration (physical mobility) are attributed to vata (and its 5 sub types).
- Digestion and metabolism (including tissue metabolism); hormonal activities are attributed to pitta (and its 5 subtypes), along with agni.
- All anabolic activities / body building are attributed to kapha (and its 5 subtypes).
- All the three doshas also have psychological attributes (as shown above)

### The sapta dhatus

The seven primordial tissue units in the body are Rasa\* (the primary starting point of dhatus, derived from the food), Rakta (blood and related haematological system), Mamsa (the flesh or muscular system), Medas (adipose or fat tissue), Asthi (bone or skeletal system), Majja (bone marrow as also the neurological system), Shukra/Shonita (reproductive system in the male/female). Each of these tissues (again 'functional' rather than 'structural or anatomical entities) is said to develop sequentially (in the order listed above), by deriving nourishment from the tissue preceding it, and getting to be more complex and subtle, and also 'higher' in the order of progression.



Thus, as shown in Figure 2, starting from Rasa (derived almost entirely from food), the dhatus (which are the physiological "building blocks") evolve finally into the most important and intricate dhatu ie. shukra, – the reproductive element (that holds the genetic blueprint of DNA) – which is considered in Ayurveda as the ultimate dhatu responsible for progeny. Ojas, in Ayurveda, constitutes the essence of all the seven dhatus and is the subtle, vital energy

\* Dr. C. Dwarkanath interprets 'rasa' as the fluid ever circulating throughout the body (like a rotating wheel) transporting nutrients to various tissues.<sup>27</sup>

responsible for conferring general immunity and long life-span (by countering/delaying, the ageing process) in human beings. The anti-ageing regimens/techniques of Ayurveda named Rasayana tantra (to which a whole chapter is devoted in Ayurvedic texts), target all the seven dhatus and their progressive nourishment, with the ultimate aim of not only improving the life span of the subject but also improving the ojas by providing special nourishment to different dhatus resulting in increased life span with superior quality of all the 'building blocks'. Each of the dhatus has its own specific agni (responsible for specific biochemical processes or tissue metabolism), which is active throughout one's life. The concept of Agni and Ama are explained in Figure 2

### **Triguna (Three primordial mental 'gunas' or characteristics)**

The trigunas (Satva, Raja and Tamas)<sup>9</sup> are psychological counterparts of the panchabhautic tridoshas (which mainly decide the 'body' make up of an individual). The three gunas (primary/basic qualities of the mind) are said to exist in different proportions and state in each human being. Satva represents purity and knowledge, Rajas represents action and creativity/passion, while Tamas represents ignorance and inertia. In other words, the quality of the mind and therefore the 'character' of a human being are decided by trigunas. Thus, a satvic individual is calm, gentle, and tolerant/forgiving, whereas a rajasic person is impulsive, passionate, and materialistic/possessive, and a tamasic person will be ignorant, insensitive, lazy, and untruthful. Some believe that the 'trigunas', unlike 'tridoshas' are not determined at birth, but are influenced by extraneous factors (including nutrition)<sup>10</sup>.

In order to understand how Ayurveda works out practical guidelines for preservation/ promotion of health by simple modifications in life-style particularly with regard to diet, a few Ayurvedic terms like Rasa, Guna, Virya, Vipāka, karma and prabhava need to be understood. These terms /concepts, in fact, encompass the entire gamut of Ayurvedic pharmacology (Dravyaguna Vignana).<sup>14</sup> Ayurveda does not differentiate between food and drugs, in terms of the ultimate 'fate' of any substance (dravya) which is ingested by (or orally administered to) a living being. Ayurvedic pharmacology thus deals with "substances" (dravyas) and not necessarily with only 'drugs'. In fact, Charaka emphatically states<sup>15</sup> that there is no "substance" in this world which cannot be used as a 'drug'!

Rasa, Guna, Virya, Vipaka, Karma and Prabhava of food items (and drugs): Rasa, in this context is quite different from the Rasa dhatu, and refers to the primary taste of the substance orally ingested. Ayurveda describes six primary rasas or tastes viz. Madhura (Sweet), Amla (Sour), Lavana (Salty), Tikta (Bitter), Katu (Pungent) and Kashāya (Astringent). Modern physiology as we know, refers to only four tastes viz. *sweet*, *sour*, *salty* and *bitter* (for which specific "taste buds" in food items and drugs, although it is the primary rasa (along with its post digestive status/effect) which is responsible for the pharmacological/therapeutic actions (karma and prabhava. Each of the six rasas again, is composed of a combination of the five primordial elements, contributing to the qualities (guna) and virya (potency) of the food items and

<b>Table 3: The twenty gunas / attributes (10 sets of opposing qualities) and their effect on tridoshas (and responsible for action of Food &amp; Drugs)</b>
<p><b>Guru (heavy) and Laghu (light)</b>  <b>Guru (Heavy) aggravates Kapha</b>, but <b>alleviates Vata and Pitta</b>; decreases or delays <b>digestibility</b>; but after digestion / absorption, promotes bulk and lethargy. <b>Laghu (light) aggravates Vata and Pitta (and agni)</b> but alleviates <b>Kapha</b>; helps in easy digestion, while reducing bulk, and promoting alertness.</p>
<p><b>Ushna (Hot) and Sheeta (Cold)</b>  <b>Ushna</b> aggravates <b>Pitta (and agni)</b> and decreases <b>Vata and Kapha</b>; promotes heat, digestion, inflammation, anger, hate etc. <b>Sheeta (cold)</b> aggravates <b>Vata and Kapha</b>, while alleviating <b>Pitta</b>; leads to cold, numbness, constriction, lethargy, insensitivity, inactivity.</p>
<p><b>Snigdha (Moist / oily) and Ruksha (Dry)</b>  <b>Snigdha</b> aggravates <b>Pitta and Kapha</b>, decreases <b>Vata and Agni</b>; responsible for moisture, smoothness, lubrication, vigour; promotes love and compassion. <b>Ruksha (Dry) – aggravates Vata and agni</b>, decreases <b>pitta and Kapha</b>; leads to dryness, constipation; nervousness / restlessness.</p>
<p><b>Tikshna (sharp / penetrating) and Manda (slow)</b>  <b>Tikshna</b> aggravates <b>Vata and Pitta</b> and alleviates <b>Kapha</b>; is responsible for quick action, may cause ulcers / perforation; promotes sharpness, grasp / understanding. <b>Manda</b> aggravates <b>Kapha</b>, alleviates <b>Vata and Pitta</b>; leads to slow action (of food / drugs), sluggishness, lassitude, dullness.</p>
<p><b>Slakshna (smooth / slimy) and Khara (rough)</b>  <b>Slakshna</b> aggravates <b>Pitta and Kapha</b>, decreases <b>Vata and agni</b>; promotes smoothness; loving and caring. <b>Khara (rough)</b> aggravates <b>Vata and Agni</b> decreases <b>Pitta and Kapha</b>; leads to cracking of skin and bones; promotes carelessness, insensitivity / rigidity.</p>
<p><b>Sandra (dense / solid) and Drava (liquid)</b>  <b>Sandra (solid)</b> aggravates <b>Kapha</b>, decreases <b>Vata and Pitta</b> promotes solidity, density, strength; integrity. <b>Drava (liquid)</b> aggravates <b>Pitta and Kapha</b>, decreases <b>Vata and Agni</b>; dissolves / liquefies; promotes hydration; compassion.</p>
<p><b>Mridu (soft) and Kathina (Hard)</b>  <b>Mridu (soft)</b>: aggravates <b>Pitta and Kapha</b>, decreases <b>Vata and agni</b>; promotes softness; relaxation, tenderness, love. <b>Kathina (hard)</b> aggravates <b>Vata and Kapha</b>, alleviates pitta and agni; increases hardness, strength, rigidity; insensitivity, selfishness.</p>
<p><b>Sthira (static / stable) and Sara / chala (mobile / flexible)</b>  <b>Sthira (static)</b> (aggravates <b>kapha</b>, decreases <b>Vata, Pitta and agni</b>; promotes stability, constipation, obstruction; faith, integrity. <b>Sara / Chala (non-static / mobile / flexible) – aggravates Vata, Pitta and Agni</b>; decreases <b>Kapha</b>; promotes mobility, flexibility; restlessness, fluctuating attachment / faith.</p>
<p><b>Sthula (gross) and Sukshma (subtle)</b>  <b>Sthula (gross)</b> aggravates <b>Kapha</b>, decreases <b>Vata, Pitta and agni</b>; promotes bulkiness, obstruction, inflexibility. <b>Sukshma (subtle)</b> aggravates <b>Vata, Pitta and agni</b> and alleviates <b>Kapha</b>; penetrating / subtle and deep in action; sharpens emotions / insights.</p>
<p><b>Vishada (clear) and Pichchila / Avila (turbid / cloudy / viscous)</b>  <b>Vishada</b> aggravates <b>Vata, pitta and agni</b> and alleviates <b>Kapha</b>; pacifies, diverts, clarifies (perception). <b>Picchila / Avila (turbid) – aggravates Kapha</b>; alleviates <b>Vata, pitta and agni</b>; promotes healing of fractures; leads to lack of clarity, perception</p>
<p>*<b>Agni</b> is a unique Ayurvedic concept exclusively referring to the intricate biochemical / enzymatic and hormonal actions / processes occurring in the body (involving digestion, metabolism; assimilation and conversion of food items and drugs). For details, see Table 1.</p>

drugs which, in turn, result in specific (often predictable) actions (karma) on the human body-mind unit (Table 3 exits in the tongue). Ayurveda also refers to anurasas (secondary tastes). Unexplained/unexpected pharmacological/therapeutic actions of certain drugs (which cannot be predicted on the basis of Rasa, Guna, Veerya, Vipaka) are termed as unique effects (or prabhava) by Charaka<sup>14</sup>. Prabhava could be in addition to or different from Karma (action).

## Guna

All substances are said to have twenty gunas (ie. 10 sets of two opposing properties), which, in turn, affect the tridoshas, in various ways (Table 4).

## Virya

Virya is a rather complex Ayurvedic concept that infers the action of a

<b>Table 4: The rasas (tastes), their (important) gunas (attributes), virya (potency), vipaka (post-digestive status of transformation) and action on tridoshas (with particular reference to foods)</b>						
RASA (Taste)	MADHURA (Sweet)	AMLA (Sour)	LAVANA (Salty)	KATU (Pungent)	TIKTA (Bitter)	KASHAYA (Astringent)
Bhautic composition (elements)	Earth + Water (Prithvi + Ap)	Earth + Fire (Prithvi + Agni)	Water + Fire (Ap + Agni)	Fire + Air (Agni + Vayu)	Air + Space (Vayu + Akasa)	Air + Earth (Vayu + Prithvi)
Gunas*	Cold (sheeta) Heavy (Guru) Moist (snigtha)	Hot (Ushna) Light (laghu) Moist (snigdha)	Hot (ushna) Heavy (laghu) Moist (snigtha)	Hot (Ushna) Light (laghu) Dry (Ruksha)	Cold (Sheeta) Heavy (guru) Dry (Ruksha)	Cold (sheeta) Heavy (guru) Dry (Ruksha)
Virya	Cooling <sup>l</sup> Moist <sup>h</sup>	Heating <sup>m</sup> Moist <sup>l</sup>	Heating <sup>l</sup> Moist <sup>m</sup>	Heating <sup>n</sup> Dry <sup>h</sup>	Cooling <sup>n</sup> Dry <sup>m</sup>	Cooling <sup>m</sup> Dry <sup>l</sup>
Aggravates	Kapha	Kapha & Pitta	Kapha & Pitta	Vata Pitta	Vata	Vata
Alleviates	Vata & Pitta	Vata	Vata	Kapha	Kapha & Pitta	Kapha & Pitta
Vipaka (Six rasas have only three vipakas)	<ul style="list-style-type: none"> <li>Madhura &amp; Lavana Rasas lead to</li> <li>Madhura Vipaka</li> <li>Amla Rasa leads to Amla Vipaka</li> </ul>				Katu, Tikta & Kashaya Rasa lead to Katu Vipaka	
Aggravates	Kapha			Pitta		Vata

l = low ; m = medium; h = high  
 \*For foods, the three major sets of 'gunas' shown here are important (for drugs, all gunas are important, in conjunction with virya).  
 On the basis of this Chart, food items (according to their Rasa / gunas can be selected for each dosha (and Prakriti). For more insights on rasa, guna, virya, vipaka, please see ref : 14 (P.V. Sharma, 1976), and ref. no. 10 (Partap Chauhan, 2000).

substance (food or drug) on the body, on the basis of its 'potency' (determined mainly by three sets of 'gunas' particularly hot/cold, heavy/light, sharp/dull), in case of food items/diet (Table 4).

In India, the general experience in both rural and urban areas is that the common man would like to know whether a particular food item is 'hot' or 'cold'! Such a query is usually treated with amusement by modern physicians/dieticians/nutritionists as well as the intelligentsia (as originating from mere folk lore or superstition). Actually, this notion has its basis in Ayurveda. Ushna (heating) and Sheetata (cooling) viryas do not literally mean an effect on body temperature or heat/cold generated by the substance. What it refers to is the physiological/metabolic effect induced by the substance ingested through biochemical reactions in the gastro-intestinal tract as also in

the post-digestive phase (vipaka). Based on its panchabhautic constitution, substance (food or drug) may become 'heating' or 'cooling'. Thus, substances with the fire (Tejas or agni) element in them (ie. with amla or sour, lavana or salty, katu or pungent rasas) will have ushna (hot/heating) virya, whereas food and drugs without the fire (agni) element (ie. madhura or sweet, tikta or bitter and kashāya or astringent rasas) will have sheeta (cold/cooling) virya.

Vipaka is the term used in Ayurveda for the 'post-digestion' status and effect of the substance orally ingested. Only three vipakas are described for the six rasas (Table 4). In other words, while Rasa-guna is responsible for the pharmacokinetics, veerya-vipaka, karma and prabhava correspond to the pharmacodynamics of modern pharmacology. As Ayurveda does not differentiate between food and drugs, in this respect, it is important (and possible) to determine the Rasa, Guna, Virya of any given substance and predict most of its karma or pharmacological actions.

With this background information on general principles of Ayurveda, we can now turn to the all-important concept of "Prakriti" – a unique practical 'strategy' offered by Ayurveda for understanding the physical/physiological-metabolic make-up of individual human beings. On the basis of the tridosha theory, Ayurveda categorizes all human beings into seven "metabolic types" or prakritis. Vata, pitta, kapha are the three primary prakritis. In practice, however, it is well known that while one dosha (ie. primary dosha) predominates, the secondary dosha also plays an important role in an individual's make-up. Occasionally, two doshas may be equally dominant, leading to dual prakritis viz. vata-pitta, pitta-kapha and kapha-vata. The seventh prakriti is a rare one viz. - the 'tridosha' or 'Sama prakriti (wherein all the three doshas are equally dominant and in balance). There is elaborate description with regard to physical/physiological and psychological categorisation of prakritis in Ayurveda.<sup>11, 12,13,16</sup>. For practical purposes, however, one needs a 'workable' formula to elicit the most essential information from each individual, in order to determine his/her "prakriti". Commendable efforts in this direction have been made by a few Indian Ayurvedic experts and also by Ayurveda experts /scholars practising outside India (particularly in the US, Germany and some in the U.K and Australia), as also by Ayurveda enthusiasts among Western medical specialists, anthropologists, and Vedic scholars – particularly from the US (inspired by Deepak Chopra and his associates)<sup>17</sup>.

These efforts, and those of Vedic scholars like David Frawley<sup>7, 19</sup> and Ayurveda experts like Vasant Lad<sup>13</sup>, Robert Svoboda<sup>12, 16</sup> and others have led to the so-called 'New Age Ayurveda' which is now flourishing as a Western 'movement', to popularise Ayurveda outside India. A sizeable number of "Ayurveda clinics" and Teaching Institutes are offering courses on Ayurveda in the US and a few other countries. Several 'self-help' and 'teach yourself' courses, websites, and publications are actively spreading the message of Ayurveda to the common man (outside India). Within India, where Ayurveda originated, however, such efforts have been made only by a few Ayurvedic experts<sup>10, 21</sup>. While the clinical practice of Ayurveda in most parts of India is flourishing, attention to Ayurveda's "preventive health" and "anti- ageing



measures” is not getting the required attention in hospitals/clinics and the daily routine of individuals.

The questionnaire given in Annexure 1 is a condensed version of what is being used widely in many Western Ayurveda clinics/institutes, and has been developed by Indian and Western or ‘New Age Ayurveda’ experts. Western medical experts (outside India) are slowly and steadily being exposed to and influenced by not only the Ayurvedic concepts of Nutrition, but also the Ayurvedic perception of ‘mind and body’ as a single unit. The questionnaire on prakriti thus tries to elicit considerable “subjective” information from individuals, to determine their prakriti. It would be natural for most experts/scholars trained in modern medicine/modern science to dismiss it as ‘highly subjective’ and therefore unreliable and unscientific. But a closer look will discern the wisdom of ancient Indian authorities who had developed extraordinary degrees of clinical acumen and sharpness of intellect along with acute powers of observation, combined with intuition. Their inferences are based on penetrating insights and long-term clinical experience (without the use of sophisticated diagnostic tools and aids available today because of the tremendous scientific and “technological advances” witnessed in the past century). For them, ‘prakriti’ was meant to be determined by close interaction with the individual, in order to guide him/her regarding life-style modifications suitable in terms of age, time of the day, season and the overall “disposition” of each subject (without the aid of sophisticated technology).

### **Qualities of primary prakritis (Vata, Pitta, Kapha)**

Individuals of Vata prakriti manifest the typical gunas (qualities) of the elements air (vayu) and space/ether (akāsha) ie. dry, rough, light, subtle, cold and mobile. Thus, they have dry hair; rough, dry skin; they are bony thin and fragile. Their sleep is light, nature restless, anxious; they are on the move, most of the time; energetic, but with low stamina and erratic/irregular in habits, appetite. Flatulence is a common problem for them. They talk fast (and enjoy talking), dislike cold, windy/dry climate (and catch cold easily). Vata individuals are innovative, sensitive, spend impulsively. Their grasp and memory are sharp, but short-lived. Most Vata individuals are intellectuals, could be non-conformists, adventurous and often loners.<sup>10, 16, 20</sup>

Those with Pitta prakriti<sup>10, 16, 20</sup> exhibit the qualities of elements fire (tejas/agni) and water (ap) elements viz. hot, light, sharp, intense, acidic/pungent. Pitta individuals are thus fiery (hot). They are of medium build, with soft and warm skin, sharp eyes, and strong appetite and digestion, and they are good sleepers. They are intelligent, with excellent grasp and memory, very clear in thinking and talking, often dominating others; they are ambitious, aggressive, competitive, decisive, far-sighted and can make good leaders. Being ‘fiery’ they are often short-tempered and critical of others. They dislike heat and sunlight, and are prone to acidity, skin rashes, allergies etc. Individuals of Kapha prakriti<sup>10, 16, 20</sup> display the qualities of elements earth (prithvi) and water (ap) viz. heavy, dense, stable, slow, cold, oily. Thus, kapha types are heavy in build, often overweight, with smooth skin, moderate / high appetite with slow digestion. They are sluggish in movement / activity and dislike physical

<b>Table 5: Classification of food in ayurveda</b>	
I.	<b>Hita (wholesome) and Ahita (unwholesome).</b>
II.	According to <b>manner of Ingestion: Edible, potable, lickable, masticable.</b>
III.	According to <b>Rasa (taste): Sweet (Madhura), Sour (Amla), Salty (lavana), Bitter (tikta), Pungent (Katu) and Astringent (Kashaya).</b>
IV.	According to <b>source / nature</b> of food items: <ul style="list-style-type: none"> <li>➤ <b>Sukhadhanya</b> (Grains with husks) i.e., cereals like rice, wheat, maize, corn, barley, Ragi etc.</li> <li>➤ <b>Samidhanya</b> - Pulses / legumes) – All dals, graded from 'light' to 'heavy' (according to their digestibility and bioavailability).</li> <li>➤ <b>Shaka</b> (vegetables)</li> <li>➤ <b>Harita</b> (greens)</li> <li>➤ <b>Phala</b> (fruits)</li> <li>➤ <b>Gorasa</b> (Milk and milk products of various animals)</li> <li>➤ <b>Mamsa</b> (Meat of various animals and birds)</li> <li>➤ <b>Madya</b> (Fermented products / wines)</li> <li>➤ <b>Ikshuvarga</b> (Sugarcane products)</li> <li>➤ <b>Jalavarga</b> (water and beverages)</li> <li>➤ <b>Kritanna</b> (cooked food / processed food)</li> <li>➤ <b>Aharayogi</b> (food supplements including cooking oils, spices, salts, nuts and seeds).</li> </ul>
V	According to psychological* action <ul style="list-style-type: none"> <li>➤ <b>Satvic</b> : Fresh fruits, vegetables (salads &amp; cooked), fresh juice, grains, nuts, seeds, water, cow's milk, honey; herbal tea.</li> <li>➤ <b>Rajasic</b>: Spicy (hot) food items, fried / baked foods, sweet meats, aerated drinks cookies; heavy pulses, onion, garlic, chillies, caffeine beverages.</li> <li>➤ <b>Tamasic</b>: Stale food, frozen or canned food; fermented food; processed food (junk food); mushrooms, garlic (in large quantity), all meat and alcohol.</li> </ul>
<b>Note:</b> *Ayurveda invariably <b>links mind and body</b> (in <b>health and disease</b> ). The <b>mental attributes (trigunas)</b> which are the counterparts of <b>tridoshas</b> are : <b>Satwa</b> (representing purity / wisdom); <b>Rajas</b> (representing activity) and <b>Tamas</b> (representing inertia / ignorance). Elaborate description of the trigunas, their qualities and impact on individual (psychological) constitution, (see Ref. 9,10 and 11) as also with regard to food items, activities / lifestyles in available in Ayurvedic texts.	

exertion; their sleep is sound and prolonged. They dislike dampness. They are slow in grasping, but have excellent long-term memory. They are stable, tolerant / forgiving and have a loving disposition, often with melodious voice and oratorical skills. They can be possessive (in love and also with respect to money).

Food and nutrition being considered one of the important pillars (upstambhas) of life, elaborate and specific guidelines were prescribed for each dosha/prakriti. Based on personal experience in the past seven years (by conducting workshops) certain dietary guidelines for Indian subjects have been worked out, incorporating

- food items available locally and
- modern knowledge on “functional foods” ie. food items with nutritional and medicinal properties. Dietary guidelines for the three primary prakritis (vata, pitta and kapha) are given in

Tables 5 and Annexure 2. These tables also indicate vulnerability of different prakritis to modern conditions like lactose intolerance, effect of trigger foods, etc.

The Ayurvedic classification of food by both Charaka and Sushruta illustrate their profound knowledge of food items, their source, quality and requirement/usage by human beings, as also food-food and food-drug incompatibilities. Strangely, while Western scholars/historians/medical experts have shown great interest in Ayurveda as a system of medicine (with valuable fundamental concepts) relevant for the current health situation, in India very few modern medical authorities, with a few notable exceptions<sup>3, 22-24</sup>, have evinced genuine interest to study Ayurveda as a complete health science (including its basic tenets). Most scientists and health/medical authorities in India still look upon Ayurveda as an alternate system to be tapped/explored only for specific “herbal drugs” which may provide cure/relief for refractory diseases or chronic conditions not amenable to “modern” medicine! However, in recent years, a few Indian Ayurvedic experts/scholars have, fortunately, authored books with special insights and interpretations of Ayurveda.<sup>10,11,21,28</sup>

On the basis of feedback received from a series of lectures -cum –workshops I have been conducting at Bangalore (with the assistance of a small team of young Ayurvedic physicians and a few Home Science graduates), I have come to believe that the Ayurvedic concepts of nutrition and the dietary guidelines worked out according to individual “prakritis” offer a scientifically sound and practical schedule for promoting/preserving a healthy lifestyle for all sectors of Indian society. This schedule can be adopted easily at home, hospitals and selected eateries like student hostels, canteens, corporate work places (with food courts), selected health restaurants etc.

I also believe that modern nutritionists/dieticians in India would benefit by being introduced to the Ayurvedic concepts of nutrition, while Ayurvedic physicians would definitely benefit by an exposure to advances in modern nutrition, especially with regard to functional foods. Charaka advised that Ayurveda is not a ‘static’ science but dynamic and progressive, absorbing new knowledge and wisdom continuously from all over the world<sup>25</sup>. The emphasis on “wellness” ie how to preserve/promote ‘good health’ through proper dietary guidelines, is mostly lacking in current Ayurveda practitioners in India (whose emphasis is mainly on “pathya-apathaya” or “dietary restrictions” prescribed for management of specific diseases). Modern dieticians/nutritionists seem to be totally disease-oriented (working out therapeutic diets specific for diseases like diabetes, hypertension, heart disease etc.). Some Western nutritionists<sup>26</sup>, on the other hand, have already adopted Ayurvedic principles and worked out recipes for different constitutions (prakriti).

### **Scope for research on ayurvedic prakriti and nutrition**

Apart from the need for epidemiological research on nutrition concepts of Ayurveda, genetic research pioneered by Bhushan Patwardhan and his team<sup>29</sup> in recent years, offers great opportunities for throwing new light on the ancient insights of Ayurvedic physicians/scholars. Patwardhan’s original work on classification of human population based on HLA gene polymorphism with correlation to the Ayurvedic concept of prakriti has led to an important national project, launched recently in India. The results of these studies are expected

to have significant implications for future research in epidemiology, pharmacogenetics and the practice of “personalised” health and medicine.

For launching controlled clinical/epidemiological studies on the nutrition/dietary guidelines prescribed according to prakriti, one need not wait for the results of the ongoing national project on genetic correlation of prakriti. Lest India be forced to borrow the results of ongoing studies on diet and prakriti from other countries, well planned and focused studies should be launched in India by nutrition experts/institutes on the Ayurvedic concepts of dietary guidelines according to prakriti.

I have fond hopes that some day (in the near future), both NFI and NIN will have an “Ayurveda research wing” to investigate, analyse and, if proved efficacious, to incorporate some of the ancient Indian wisdom in the national policies of food and nutrition in our country. To assess the benefits of applying Ayurvedic concepts/practices of nutrition for positive health, controlled long-term studies on the Indian population at regional/national levels are called for. The venerable Charaka<sup>30</sup> himself stated that – ancient or modern- “the wise should not accept anything without investigation” and these wise words of Charaka have been incorporated (since the 1960’s) in the insignia of the Indian Council of Medical Research. It would also be wise and important, in my view, to select topics for such investigations and decide their relative priority. The place and time for launching investigations on nutrition according to prakriti is here and now!

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<b>Questionnaire to identify prakriti (Human Constitution)</b>			
<b>Characteristic</b>	<b>Vata</b>	<b>Pitta</b>	<b>Kapha</b>
Frame	Thin	Moderate	Large
Body weight	Low	Moderate	Heavy
Skin	Dry, Rough, Cool, Brown	Soft, Oily, Warm, Fair, Red,	Thick, Oily, Cool, Pale
Hair	Black, Dry, Kinky	Soft, Oily, Yellow, Red Early gray	Thick, Oily, Wavy, Dark or Light
Teeth	Protruded spaces between teeth; crooked: gums emaciated	Moderate in size, soft or bleeding gums	Strong, White; gums, well-formed
Eyes	Small, dry, active, Brown, Black	Sharp, Penetrating, Green, Gray,	Big, Attractive, Blue; Thick, eyelashes
Appetite	Variable, Low mostly	Good, Sharp, excessive	Slow but steady & strong (can withstand fasting)
Disease Vulnerability (pre-disposition)	Neurological and stress disorders; gas in abdomen, pain etc.,	Acid indigestion, skin rashes, infection, inflammation	Water retention, mucus secretion, respiratory congestion, obesity-related disorders.
Thirst	Variable	Excessive	Low
Bowel movement	Dry, Hard, stools; constipated	Soft, Oily, Loose/ copious stools	Thick, Oily, heavy stools; slow motion
Physical activity	High (mostly on the move)	Moderate	Lethargic (Dislikes Physical activity)
Sleep	Light, interrupted	Short, but sound	Deep & prolonged
Attachment / Loyalty	Variable / Shifting	Intense & extreme; (averse to easily forget & forgive)	Deep & consistent (can be possessive)
Preferences for rasas / tastes (in food)	Sweet ( <b>Madhura</b> ) Sour ( <b>Amla</b> ) Salty ( <b>Lavana</b> )	Sweet ( <b>Madhura</b> ) Bitter ( <b>Tikta</b> ) Astringent ( <b>Kashaya</b> )	Bitter ( <b>Tikta</b> ) Pungent ( <b>Katu</b> ) Astringent ( <b>Kashaya</b> )
Preference for music*	Variable; instrumental preferred; Also likes group music; rhythmic tunes; sometimes soft music	Exciting / noisy / loud; racy music; Group singing and group dances; folk music	Soft and romantic music; likes Classical and devotional music (Bhajans), with good lyrics.
Dreams*	Flying jumping running, fearful	Fiery, angry, passionate, colourful	Watery, ocean, swimming, romantic
Speech	Fast, Uninterrupted, Not very clear, but full of new ideas	Sharp, Clear, cutting, incisive, (make good leaders)	Slow, monotonous (with long gaps) but melodious voice, often good orators
Spending habits*	Spends quickly, impulsively	Spends moderately & methodically	Spends slowly; saves (after careful planning)
MIND (Mental qualities)	Restless, creative, curious, inquisitive, mentally very active	Intelligent, sharp, aggressive, active most of the time;	Calm, slow, receptive, (but seemingly dull)
	Creative thinker, innovator, non-conformist	Good initiator and leader	Seemingly dull; good organizer & co-ordinate
	Dislikes routine (very restless)	Enjoys planning and instructing others,	Likes routine work, within an organized frame work

		(but may not take kindly to unwanted instructions!)	
	Not disciplined nor always focused, (dislikes to submit to discipline)	Disciplined (within one's own orbit) and expects total discipline from subordinates	Disciplined (dislikes indiscipline in others)
	Changes mind easily (His /her priorities seem to shift periodically)	Has strong opinions and likes to share with (and possibly impose them) on others.	Slow to form and change ideas or opinions, but firm once decided; but lethargic in expressing opinion
Emotions / Temperament	Mostly Insecure and anxious; under stress, tends toward anxiety, fear and nervousness	Confident; under stress, tends towards irritability, anger and frustration; expects obedience / compliance from others	Tends to avoid stress and difficult situations but once confronted, faces stoically, without faltering
Memory	Recent memory Sharp; remote memory poor	Sharp & distinct recent memory; Selective / long term memory:	Slow and distinct (rarely forgets, once memorized)
Intellect	Very quick, impulsive, (can be faulty)	Sharp & accurate (quick in grasping)	Slow, but exact and sound

<b>Dietary guidelines according to Prakriti</b> <b>Dietary guidelines for vata prakriti</b> [Madhura (Sweet); Amla (Sour) and Lavana (Salty) are good for Vata Prakriti]		
	<b>USE</b>	<b>RESTRICT / AVOID</b>
1. Cereals (Grains)	<b>Cooked Rice, Wheat, Oats, Ragi</b>	No Corn Maize, White bread
2. Pulses (Legumes)	<b>All pulses produce excessive gas in Vata individuals)</b> Hence to be used only in moderation. <b>Moong Dal, Toor Dal, Udad, Soya Bean</b>	All “raw” ie., uncooked dals; to avoid / restrict <b>chana, peas rajma, horsegram, heavy</b> (guru), beans
3. Vegetables	Cooked <b>Carrots, Beetroot, Sweet potato, Green beans, radish, onion, sweet corn, capsicum</b> (cooking with some oil / fat is good for vata, but not frying)	<b>All “raw” (uncooked) vegetables (salads)</b> to be restricted / avoided. To restrict <b>cabbage family vegetables</b> ; moderate use of leafy greens & sprouts permitted. Potato / Tomato family vegetables (to be tested for “trigger” effect)
4. Fruits	<b>Generally, all sweet and slightly sour fruits.</b> Banana, berries, grapes, citrus, fruits (lemon, orange, mosambi), mango, sweet melons, papaya, pineapple, peaches, plum, guava (in small quantities)	<b>(To restrict fibrous and highly sour fruits)</b>  Dry fruit, raw apple, pears, sour melons, pomegranate
5. Spices	<b>All spices in moderate quantity.</b> Coriander, Curry leaves, femug reek, turmeric mustard, jeera, snafu, ajwain, ginger, garlic, hing mint, cinnamon, cardamom, etc. (fresh ginger tea is good for both vata and pitta)	
6. Nuts & Seeds	<b>All nuts in moderation.</b> (i.e., Almond, Cashew, Apricot, peanuts, etc.). Seeds : Flax (Agase), Yellow Pumpkin, gingili.	
7. Oils	<b>All oils in small quantities are good (to choose according to body weight, cholesterol levels and blood pressure)</b> To alternate <b>ground nut oil / sesame oil / sunflower oil</b> (olive oil to be used periodically)	
8. Dairy Products	<b>Milk, Butter, Ghee, Cheese, Yogurt</b> (in moderation). <b>(Look for “Lactose intolerance” among Vata individuals)</b>	
9. Animal Foods	White Meat (Beef, Chicken, Turkey), Eggs, Sea Food, Oily Fish.	



<b>Dietary guidelines for pitta prakriti</b>		
Madhura (Sweet); Tikta (Bitter) & Kashaya (astringent) rasas are good for pitta		
	<b>USE</b>	<b>RESTRICT / AVOID</b>
1. Cereals (Grains)	<b>Rice, Wheat, Oats, Barley</b>	<b>Corn, Millet, Ragi, Rice</b>
2. Pulses (Legumes)	<b>Most legumes are good for pitta</b>	Rajma / Horse Gram
3. Vegetables	<b>Mostly sweet and bitter astringent</b> Cabbage family: (cabbage, cauliflower, broccoli turnip, Knol-khol, green beans, leafy greens, lady's finger, peas, potato, red pepper (capsicum), cucumber etc., sweet potato (in small quantities).	<b>All Pungent (Katu rasa)</b> Brinjal, Radish, Onion / Garlic, Carrots, Capsicum, Spinach, Mushroom to be restricted. <b>(Tomato family to be tested for "trigger" effect)</b>
4. Fruits	All "Sweet" fruits permitted Apple, avocado, sweet orange, mosambi, mango, sweet papaya, sweet pineapple, pomegranate, melons, guava (small quantity)	<b>"Sour"</b> fruits restricted. Berries, Banana, Grapes, Lemon, Orange (Sour), Peaches, Pineapple (Sour), Plums, Mango, Raisins
5. Spices	Only small quantities of coriander Cardamom, cinnamon, fennel, turmeric, fresh ginger	As " <b>Pitta</b> " itself is hot (fiery), strong spices (with fire element), especially dry ginger, chilies, mustard, must be restricted / avoided.  <b>(Restrict salt for Pitta Prakruti)</b>
6. Nuts & Seeds	<b>No nuts except coconut.</b> Seeds – Pumpkin, sunflower and small quantity of flax seeds in ground form	
7. Oils	Sunflower, Olive, groundnut, soy, coconut oil (only for seasoning)	Sesame Oil Safflower oil Corn oil <b>(Restrict / Avoid frying in any oil)</b>
8. Dairy Products	Unsalted butter, ghee, milk, sweet yogurt (non-fat)	Sour Cream, Yogurt (sour), Buttermilk, Cheese
9. Animal Foods	Only white meat (Chicken or turkey), egg white, shrimp, oily fish	Beef, Lamb, Pork and seafood

<b>Dietary guidelines for kapha prakriti</b>		
Katu (Pungent, Tikta (bitter)& Kashaya (astringent) rasas are good for Kapha Prakriti)		
	<b>USE</b>	<b>RESTRICT / AVOID</b>
1. Cereals (Grains)	Rice (small quantity), Corn, Oats (dry), Barley	All refined carbohydrates like <b>white rice, wheat, maida, white bread etc.</b>
2. Pulses (Legumes)	Most pulses can be freely used	Soya products
3. Vegetables	Raw vegetables / Salads Cabbage family, Leafy greens, Bitter Gourd, beans, brinjal, raddish, onion, lady's finger, capsicum, spinach, lettuce, mushrooms	
4. Fruits	All astringent & fibrous fruits recommended Apple, Pears, Berries, Cherries, Dry Fig, Prunes, Peaches, Guava	Sweet & Sour fruits Banana, Avocado, Grapes Lemons, Melons, Oranges, Papaya (Ripe)
5. Spices	All spices are good particularly black pepper, chillies, ginger, turmeric, jeera, ajwain, fennel, mint, coriander, cinnamon, hing.  (Dry Ginger Tea for Kapha)	Salt to be restricted
6. Nuts & Seeds	Seeds Yellow pumpkin seeds and flax seeds, (powder) in small quantity	No nuts at all (Particularly Almonds, Cashew nuts, walnut, peanut, coconut to be avoided)
7. Oils	No Fried food	Restrict all oil to small seasoning (Frying / deep frying strictly forbidden)
8. Dairy Products	No Dairy product Only goat's milk advised occasionally; non-fat buttermilk.	Yoghurt
9. Animal Foods	White meat (chicken and turkey) Eggs, Fish (fresh Water)	Beef, Lamb, Pork (all dark meat).

## **ENHANCING IRON AVAILABILITY FROM INDIAN MEALS: SOME INTERESTING OBSERVATIONS FROM OUR STUDIES**

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*It is indeed an honour to be invited to contribute to this volume to felicitate Dr. Gopalan on his 90<sup>th</sup> birthday, for his long, dedicated and indispensable contribution to nutritional sciences and for being a beacon of guiding light and a source of great inspiration to nutrition scientists like me. Unlike many other contributors to this volume, I came into the nutrition field rather late. I was introduced to Dr Gopalan, in 1980, by Dr Tara Gopaldas, the then Head of the Department of Foods and Nutrition at M S University, Baroda, where I had been teaching for some time and had just begun to take a serious interest in nutrition research. It was Dr. Gopalan's spontaneous and warm encouragement about a presentation I made in the Dietetics conference in 1980, where he was the chief guest that provided the best incentive for me to engage in the quest for solutions to some of the pressing nutritional problems in India. From then on it has been an immensely fruitful association that has contributed very significantly to my own professional growth and development. His deep insights into the changing nutrition scene in India and the commitment and dedication he has inculcated into nutritionists like me, by his highly disciplined and perceptive approach to the myriad problems in the field of nutrition, has been a profound influence on my own thinking and practical approaches. Dr. Gopalan is not given to complimenting people easily but when he does you know you have truly deserved it. I have fond memories of those precious occasions. I feel truly privileged to contribute to this volume, which is dedicated to Dr. Gopalan.*

### **Introduction**

Iron by virtue of its reversible states of oxidation plays a very important role in human metabolism and hence in human health. Iron containing compounds in the body can be broadly categorized into those that serve a metabolic or enzymic function and the iron that serves as a storage component. A variety of iron compounds that serve metabolic or enzymic functions are present in the body and these include haemoglobin in the red cells, myoglobin in the muscles, and the cytochromes and several other proteins that function in the transport, storage and utilization of oxygen. Depending on the stage of development the iron present in these compounds may vary from 25-55mg per kg body weight of which more than 80 % is in haemoglobin making it quantitatively the largest component carrying iron. The storage iron component accounts for 5-25mg iron per kg body weight primarily in the form of ferritin and hemosiderin, and on an average is about one gram in an adult <sup>1</sup>.

A remarkable feature of iron metabolism is the ability to conserve and re-utilize iron once it is absorbed into the body. The amount of iron absorbed each day is only a fraction of the total dietary iron but the amount absorbed varies considerably depending on the body iron stores, form and amount of iron in foods and on the combination of foods in the diet. Thus, an array of

factors influences iron absorption, some of them positively while many affect it negatively. It is the balance of these various factors that really determine how much iron we absorb. If the amount of absorbed iron is far lower than the requirement then iron deficiency sets in eventually leading to anemia.

It is a general observation that in the absence of any other iron losses from the body, the storage iron and the ability of the body to conserve the iron avidly once absorbed, can sustain our haemoglobin levels normal over several months. Therefore even under conditions of dietary iron deprivation, it takes a while for anaemia to occur. Despite this, iron deficiency and anaemia are major public health problems affecting an estimated two billion people the world over, most of them in the developing world, making it the most prevalent nutritional disorder in the world.

This wide spread iron deficiency occurs due to four major factors:

- Low intake of iron
- Low bio availability of the dietary iron
- Increased requirements during certain stages of life, such as infancy, pregnancy and adolescence
- Loss of blood either due to physiological reasons or due to infections and infestations.

All our past efforts have been focused on bridging the gap between requirement and dietary intakes by increasing iron intake through the inclusion of iron rich foods or by way of iron supplements in chemical form. We have a major national nutrition programme for the control of anaemia in pregnancy, under which iron and folic acid supplements are provided to all pregnant women from the under privileged sections at 100 mg iron and 0.5mg folic acid per day for 100 days in a pregnancy<sup>2</sup>. This is an important short-term strategy to control anemia, especially in pregnancy, when iron requirements are increased enormously and cannot generally be met through the diet alone. Similarly, there is a provision for iron supplements for pre school children, adolescent girls and lactating women in the national policy although in practice these are pursued with varying degrees of regularity. A long-term strategy for the general population would be to promote both the dietary intake of iron and its bioavailability so that the dependence on supplemental iron can be reduced. Some important issues concerning dietary iron bioavailability and how this can be enhanced in an Indian diet is the main theme of this paper.

### **Definition of iron bio availability and factors influencing it**

Bioavailability of iron is defined as the fraction of iron absorbed and utilized for specific functions such as in the synthesis of haemoglobin, heme containing enzymes and other iron containing functional proteins<sup>3</sup>. There are two major chemical forms of iron in a mixed diet, and each is absorbed by a different mechanism. Heme, that contains iron in a porphyrin ring structure, is found in haemoglobin and myoglobin and accounts for nearly 40 % of the iron present in animal tissue including fish and poultry. Because of the porphyrin ring

structure, the iron in heme containing molecules is protected from the action of complexing agents present in the meal and is taken up by the mucosal cells as the intact protoporphyrin complex. Absorption of heme iron is therefore high averaging 15 % in iron replete individuals to 35 % in those lacking iron stores<sup>4</sup>. The other chemical form of iron, namely non-heme iron is present largely in foods of vegetable origin and in non-cellular animal foods such as eggs and dairy products. In addition, approximately half of the iron in meat, fish and poultry is non heme. The specific rate of non heme iron absorption depends upon other dietary constituents ingested concomitantly as well as the iron status of the individual and ranges widely from 2-20 % depending on the above two determinants<sup>4</sup>.

The various dietary factors affecting non-heme iron bioavailability can be divided into two broad categories: the enhancers, which increase iron absorption and the inhibitors that reduce, iron absorption from the intestine. The major enhancers of iron absorption are only two; ascorbic acid and flesh foods like meat, poultry and fish, where as the inhibitors far out number the enhancers, especially in the Indian dietaries. These include tea and soy products that have the highest negative effect followed by calcium phosphate salts, egg yolk and wheat bran that also affect iron absorption negatively but not as much as tea. The other inhibitors in the Indian dietaries are phytates and fiber present in whole grain cereals and pulses<sup>5</sup>. Meat and flesh foods in addition to containing better bio-available iron; also possess the ability to enhance non-heme iron absorption from primarily vegetarian diets<sup>6</sup>. The potency of 100g of cooked meat in enhancing iron absorption has been graded as equal to that of 100mg ascorbic acid<sup>7, 8</sup>. Given the vegetarian habits of the people and the economic constraints to the consumption of flesh foods among the non vegetarians, the only enhancer of significance in the predominantly vegetarian Indian dietaries is ascorbic acid. The major findings of ascorbic acid effect on iron absorption are quite consistent as reported by several authors<sup>9-11</sup>.

- Ascorbic acid enhances iron absorption from both low and high bioavailability meals, when added as crystalline ascorbic acid or from food sources.
- The magnitude of increase is much higher in the low availability non heme iron containing meals than in the high availability heme iron containing meals.
- The increase in absorption that occurs with ascorbic acid is influenced by the ascorbic acid to iron molar ratio, larger the ratio, higher the absorption.
- Further the ascorbic acid effect has also been shown to be dose dependent, up to a level of 1000 mg. However, the enhancing effect of ascorbic acid at lower dose level is much higher than the enhancing effect at higher levels.

Thus although dose dependent, it is not necessary in practical diets to have high levels of ascorbic acid to bring about a significant increase in absorption of iron. In vivo absorption studies have shown that 30 mg of ascorbic acid can increase the iron absorption two-fold while 50-75 mg can bring about 3-5 fold increases in iron absorption. One of our studies has shown that 100mg

ascorbic acid in the form of a tablet given to anemic pre school children with lunch and dinner meals brought about a significant improvement in haemoglobin levels<sup>12</sup>. In other words with in the range of physiological intakes of ascorbic acid, iron absorption especially from typical non heme iron containing diets can be increased very significantly.

We have a variety of fruits in India that are excellent sources of ascorbic acid but at the same they may also contain varying quantities of iron absorption inhibitors such as polyphenols, and oxalates. Therefore we carried out a series of studies to assess iron bio availability from a typical wheat based Indian meal with the addition of various fruits in order to assist in formulating optimum dietary practices to improve iron status. These included a number of in vitro iron availability studies and some hemoglobin repletion studies which have provided evidence that low iron bio availability is indeed a critical factor for the poor iron status of the population thus emphasizing the need to include this in our approach to address the problem of iron deficiency anemia.

Among the several methods for estimating iron bio availability, such as the intrinsic and extrinsic tracer studies, use of stable isotopes, hemoglobin repletion and the in vitro methods, only the last two offered the scope for wide employment with out necessitating expensive and advanced laboratory facilities. We validated the in vitro procedure against the available in vivo findings<sup>13</sup> and established that it was a good screening tool for assessing the potential of various food sources for their ability to promote iron absorption<sup>14</sup>. The enhancer inhibitor effects in vitro were also consistent with the available in vivo findings<sup>15</sup>

### **Observations from the in vitro studies**

A series of in vitro iron availability studies were carried out using the method standardized and validated in our laboratory. The standard meal chosen for studying the effects of different fruits was a commonly consumed dish of Gujarat, the wheat bhakris. The recipe for wheat bhakri was standardized and the bhakris were analyzed for ascorbic acid and inhibitor content in each series. A whole range of fruits were selected from the food tables. The ascorbic acid and the major inhibitor content of these were also determined in the laboratory. The selected fruits included

- Amla (*Emblica officinalis*),
- Ber (*Zizyphus Jejuba*),
- Grapes black (*Vitis viniform*),
- Grapes green (*Vitis viniform*),
- Guavas (*Psidium Guajava*),
- Goras amla (*Pthacellobium dulci*),
- Mango ripe (*Magnifera indica*),
- Pine apple (*Anans comosus*),
- Pomegranate (*Punica granatum*)
- Orange (*Citrus aurentium*),
- Raspberry
- Sapota

The fruits were added at a level of 30g/60g and 100g for the wheat bhakri meal containing 5 mg of iron. Significant enhancement in the iron bioavailability was observed with several of the fruits<sup>16</sup>. The iron availability of the basal meal was only 4%. All the fruits except Amla, and Goras amla increased the available iron from the bhakri meal at 30g level. Amla and Goras amla produced a reduction in the available iron that appeared even more prominent when amla was added at a higher level. The reduction appeared to be due to the high content of oxalates and tannins in amla. In the case of other fruits, increasing the level of the fruit resulted in further increase in available iron but of a smaller magnitude. These observations carry important implications. A 30 g addition of most fruits that are moderate to high in ascorbic acid is effective in increasing the iron availability in typical wheat based meals. Exceptions are the ones, which have high levels of polyphenols.

### **The hemoglobin repletion study**

The in vitro assessment of iron availability serves a useful purpose of determining the food sources that have the potential to enhance iron absorption and to study the interactions between the enhancers and inhibitors. In order to know the effect in vivo, it has to be followed by either absorption studies or by hemoglobin repletion in anemic subjects. Since Guava fruit was effective in increasing in vitro iron availability, this was chosen for assessing its effect using hemoglobin repletion in anaemic adolescent girls. Further Guava fruits are liked, consumed commonly in rural and urban areas and it is easily available making it a popular fruit.

A large sample of 180 young women was screened for haemoglobin levels. Of this 40 who were anaemic were randomly assigned to the control (20) and experimental (20) groups. Base line data on hemoglobin and dietary intakes were obtained by standard procedures from all the subjects. The experimental group consumed 100 g guava fruit with the lunch and dinner meals. Compliance was checked every day. At the end of 30 days of intervention, haemoglobin levels were repeated. Anthropometric data were obtained at base line.

The subjects ate primarily a wheat-based diet in all the three meals. Breakfast consisted of bread and butter, vegetable sandwiches, vegetable puff or rice flakes upma and a cup of milk or tea. Lunch and dinner meals consisted of wheat chapattis, dal, and some cooked vegetables. Salad was usually of raw onions while fruit consumption with the meal was rare but did occur in between meals. Mean iron intake of the subjects was 9 mg/day, only 30 % of the recommended allowance for this group. Two thirds of the intake was contributed by lunch and dinner (3.1 and 3.3 mg respectively). Mean ascorbic acid intake from the lunch and dinner were 27 and 23mg per day. Tannins from the meals averaged 360 mg per day, primarily from tea, and oxalic acid intake was 82mg/day. Guava fruit consumption contributed additional 27mg oxalic acid but no tannins. Substantial amount of ascorbic acid was added to the two meals by Guava fruit, 232 mg per meal. The ascorbic acid to iron molar ratio was thus 25:1.

The outcome proved very interesting. While the fruit supplemented group increased their haemoglobin from initial 10.7g/dl to final 12.9g/dl, the control group showed a small increment of 0.3 g /dl, from 11.0 to 11.3. The net increase of 1.9 g/dl in the experimental group compared to the control was highly significant statistically as well as physiologically. Except for one subject in the experimental group who did not show any change in the hemoglobin all others increased their haemoglobin by 1-3 g/dl by the end of one-month supplementation. In the control group 39 % showed a decline in haemoglobin while the rest showed an increase less than 1g/dl. There was thus a consistency in the trend of improved haemoglobin levels in the fruit supplemented group.

Further the amount of iron absorbed in the fruit supplemented group was computed using mean body weight and reported blood volume data for this age group. The mean body weight of the subjects was 46.9 kg. Using a reported blood volume of 60ml/kg from the literature, the iron content of haemoglobin of 0.314%<sup>17</sup> and the rise in hemoglobin of 2.2g/dl, the amount of iron incorporated into haemoglobin was 193mg. The mean daily dietary intake of iron during the same period was 282mg. The ratio of the two was considered as the amount of iron absorbed, the assumption being that all iron absorbed was incorporated into haemoglobin. This was supported by serum ferritin data on the subjects, which showed no change during the one-month intervention period.

The estimate of absorption obtained by this calculation was 63%. Interestingly, we found references to similar level of absorption in iron deplete subjects in the literature though with much higher level of ascorbic acid. In a study by Cook et al<sup>18</sup> seventeen subjects were given a dose of 1g of crystalline ascorbic acid with a standard meal and iron absorption was measured using radio labeled iron. The four iron deplete subjects were reported to absorb 65.2% of the iron while in the iron replete subjects the mean iron absorption was only 9.98%. More recent studies from the St Johns Medical College in Bangalore<sup>19</sup> have also reported high levels of iron absorption in iron deplete subjects, when given crystalline ascorbic acid with a rice based meal in the ascorbic acid to iron molar ratio of 2:1 or 4:1. What is striking about our study is that natural foods that we consume day to day have the capacity to increase iron absorption several fold especially if we are iron deplete, to meet our requirements. Such a food-based strategy is pleasant, highly acceptable and does not have any unpleasant side effects as in the case of pharmaceutical iron supplements.

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# TOXICOLOGY PROCEDURES IN FOOD AND DRUG SAFETY

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## Introduction

It is an indisputable fact that no activity on earth, including something as basic as eating food, is devoid of risk. In addition, even those that are considered safe foods for consumption could be unsafe beyond certain limits. Ultimately, recommendations are made based on a risk–benefit analysis, and if the benefits largely outweigh the risks, then such foods can be recommended. But this is only provided we know that the risk assessment is based on scientifically conducted studies, and we also know the dose/quantity above which it can cause a toxic effect. To generate such information, it is very important to design and execute scientifically valid safety protocols. Animal studies are required for establishing both safety and efficacy before we conduct clinical trials in humans. Study designs are sometimes pre-determined by regulatory authorities like the Department of Biotechnology or Drug Controller General of India.

The study design should be based on a protocol to address a risk: benefit ratio. If we need to do a safety study, we require the following information:

- is there a need for this drug/food?
- what additional benefits do we get if it is used, and is it worth that risk?
- what are the details regarding its basic structure, chemical composition and mechanism of action; is there a comparator against which we could compare this new food to determine whether it is better/ not better than an existing drug/vaccine/food component?
- how is it useful and how do we measure its usefulness? This helps in establishing efficacy parameters, which are necessary before one can assess the risk and carry out pre-clinical studies. It is a prerequisite for justifying further safety studies in the field.

## Safety studies

### ***Acute toxicity studies***

The studies are very often done in rats/mice, and in either one species or two. If two species are used, one of them would be a non-rodent. The route would be the same as the intended one. If the intended route of administration is oral, then the test has to use the oral route only. The quantity and frequency of the amounts or doses to be given to the animal would depend on the human dose. In case the human dose is 1mg/kg body wt., then the equivalent dose for a rat would be 6.0mg/kg body wt and for a mouse 12.0mg/kg body wt., based on body surface area calculations. The animals would be given 10 times the human dose, i.e. 60 mg/kg per rat and 120 mg/kg for a mouse. If the human dose is not precisely known, then dose-ranging studies can be done, and animals may be given doses 1X, 5X, 10X, 100X, and so on. Such dose

escalations are useful in determining the “No observed adverse effect level” (NOAEL) or “Low observed adverse effect level” (LOAEL) <sup>1,2</sup>.

The purpose of acute toxicity studies is also for determining the margin of safety between the maximum human dose or consumption and the level at which toxicity is observed. Acute toxicity studies also provide information about the possible toxicological changes that may occur. This, in turn, would assist the investigator to specifically look for such changes during the long-term studies. In case of genetically modified crops, since it is not practically possible to feed an animal ten times more food than what it can eat, it has been decided to perform the acute toxicity test using the purified form of the protein that arises out of the inserted gene. Such proteins can be produced in significant amounts, either by an extraction process from the plant part that contains the maximum extra protein, or by using the yeast or bacterial system. The gene is then inserted into the yeast or bacteria and, by a process of fermentation and subsequent purification; adequate quantities of the pure protein can be obtained. This pure protein is then compared with a naturally occurring GM protein in the plant for its sequence homology as well as efficacy. Once it is established that the pure protein is exactly similar to the one present in the GM plant, it can be fed in quantities many-fold higher than what any human or animal can consume by feeding on the genetically modified plant sources. For GM proteins, the maximum limit given to the rodents is 2g/kg body wt. Similarly, acute toxicity studies can be performed even for novel foods or foods that are to be consumed in quantities much greater than is normally done, as in the case of fenugreek, where such studies are taken up for assessing cholesterol/glucose absorption.

### ***Chronic toxicity studies***

Once acute toxicity studies are done, the acceptability of test material is determined, and long-term studies are then planned <sup>3, 4</sup>. This may be of durations ranging from 28 days to 180 days, and are termed as ‘sub-chronic studies’ or ‘chronic studies’ depending on the duration. The duration of the study is fixed based on the proposed use of the test material/feed. If it is a food substance and is likely to be consumed for long periods of one's life, it is very essential to conduct chronic toxicity studies extending up to 180 days or even 210 days. However, if it is a drug or a possible toxin that is likely to be ingested for a much shorter duration, then 28 days of testing should be adequate. The dose of the test material is given as:

- At 1X, which is a therapeutic dose or the dose at which it is consumed or expected to be consumed by a human or an animal per day and
- 5X and 10X

There is generally no need to go beyond ten times the therapeutic dose in sub-chronic and chronic studies. The control shall have the vehicle or a non-GM food as the case may be. It is also preferable to have some studies, for about 2-4 weeks, on animals that survive beyond the period of administration of the test material with the purpose of seeing whether any changes that might have occurred because of the test material could be reversed after

discontinuing it. In case there is already a material in the market that is biologically similar or identical to the test material, and if such a material has already undergone a detailed toxicological analysis in another country, then an additional group with that innovator product is included in the sub-chronic study for comparison. Whereas in acute toxicity studies only observational parameters are taken note of at the end of the two-week period, in sub-chronic and chronic studies a detailed analysis of the clinical signs and symptoms, the behaviour, clinical chemistry, haematology, necropsy, histopathology and immunotoxicology investigations are done. The observed changes have to be analyzed to see whether they are significantly different from the control group, whether the values are within the normal physiological range, and whether there is a dose-dependant phenomenon. Based on the data from the sub-chronic studies, if there are evidences of any reproductive organ involvement, reproductive toxicity tests have to be done. If the product is likely to be used or consumed by pregnant women, it would be mandatory to do reproductive toxicology. Similarly, carcinogenicity studies need to be done for products, which are used for longer periods of time, as is the case with antidiabetic drugs. Data from carcinogenicity studies are not essential to get approval for clinical trials; they can run in parallel, since the duration of such studies would be approximately 24 months. Other specialized investigations include genetic toxicology, immunotoxicology, and allergenicity studies.

### **Safety of genetically modified food**

In assessing the safety of genetically modified crops or foods, one of the major concerns is whether the product of the inserted gene could be an allergen. The following step-wise approach is recommended for carrying out allergenicity studies<sup>5</sup>:

- find out if the source of the gene is from a known allergen
- compare the amino acid sequence of the gene product with the amino acid sequence of known food allergens or aero allergens through database searches.
- establish that the gene product is digestible in acid pepsin, since it is well known that most allergens resist acid pepsin digestion
- check the thermal stability of the protein.

Many allergens are thermally stable and persist even after cooking and processing. Evidence of allergenicity can be discerned to a certain extent during the sub-chronic study investigations as well. If there is a possibility of a test material being an allergen, the subsequent tests like ELISA test using serum from patients having known allergies i.e. targeted serum test, or double-blind placebo-controlled food challenge studies may have to be done. At the end of the entire pre-clinical safety testing process, one is reasonably certain that when the test material is administered to human volunteers in Phase 1 studies, the possibility of any toxicity occurring is negligible. Though several *in vitro* systems have been tried out as alternatives to animal use for safety testing, till date no such validated *in vitro* tests have been possible. Preclinical toxicological/safety testing procedures are the gold standard as on

date. Most of these procedures have to be done under strict quality standards, and one such internationally accepted standard is Good Laboratory Practice (GLP) accreditation given by Organization for Economical Cooperation and Development (OECD)<sup>1, 2</sup>.

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# CANCER IN WOMEN: PATTERNS AND TRENDS

Shanta<sup>1</sup> V and Swaminathan<sup>2</sup>R

## Introduction

From a global perspective, there are marked geographical variations in incidence, overall pattern of incidence of cancers, common cancer sites, and their ranking according to prevalence rates. These differences in prevalence patterns are attributable to distinctive environmental factors including socio-economic variables, personal habits such as the use of tobacco and alcohol, life-style factors including dietary habits, exposure to infection and occupation. Over the past 50 years, the study of variations in cancers occurring worldwide has given indications of possible causative factors. A study of the distribution

Registry	Cumulative risk (0-74 years)	Registry	Cumulative risk (0-74 years)
Affluent Countries		Less Developed Countries	
US, SEER, White& Black	One in 3	Philippines	One in 5
Canada	One in 3	Colombia, Cali Canada	One in 5
UK, Oxford	One in 4	Pakistan, South Karachi	One in 5
Finland	One in 4	Thailand, Chiang Mai	One in 6
Japan, Miyagi	One in 5	Malaysia, Surawak	One in 8
		INDIA	One in 8

of cancer worldwide has shown that there are two distinct groups the more developed or affluent countries and the less developed or developing countries. A comparative analysis shows that the overall incidence of cancer, the common cancer sites, the risk factors, sex ratio of cancer patients, and even survival rates, differ significantly between the two groups. The lifetime cumulative risk (0 – 74 years of age) of cancer in women in India is 1 in 8<sup>1</sup> whereas in the affluent countries it ranges between 1 in 3 and 1 in 5<sup>2</sup> (Table 1).

## Cancer incidence in women worldwide

The crude incidence of cancer in women is lower in the Indian Registries,

COUNTRY	CIR	ASR	COUNTRY	CIR	ASR
Affluent			Less developed		
US, SEER, White	467.7	295.7	Malaysia, Sarawak	94.0	120.5
UK, Oxford	389.0	232.9	Thailand, Chiang Mai	172.8	155.7
Finland	413.1	221.3	Philippines, Manila	138.6	205.0
Japan, Miyagi	371.1	187.2	Zimbabwe, Harare, African	87.0	194.9
			INDIA	90.4	112.5

even lower than in many developing countries, and significantly lower than in

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the affluent countries. The CIR and AAR in women in urban India<sup>1</sup> is 90.4 and 112.5/100,000 population in 2005 [in many developing countries it is 111.0 and 128.8, respectively, whereas in affluent countries it is 377.9 and 228.0, respectively<sup>2</sup> (Table 2).

The major problem that India faces is that, despite the lower incidence, the burden of cancer is high, which is essentially a demographic effect. It very clearly stresses the importance of population control as a major component of cancer control. Over the past two decades the CIR of cancer in women has shown an annual 1% increase, from 78.4/100,000 population in 1985<sup>3</sup> to 92.2/100,000 in 2004<sup>1</sup> (Table -3). In terms of the burden of cancer, the increase has been an alarming 79.1% (from 278,000 in 1985 to 498,000 in 2005). The trend in the affluent countries also shows an increase but the demographic effect, which is pronounced in India, is not seen in the affluent countries. In addition, the increasing trend in the affluent countries is a result of earlier diagnosis as is evident from the decline in mortality. In India and all developing countries, locally advanced disease at all sites accounts for more than 60% of the patients seeking treatment, and therefore mortality rates are high. The stage distribution of common cancers in India over the past 3 decades has not shown any significant changes, highlighting the inadequacy of effective cancer control.<sup>4</sup>

	CIR	Incident Cases Per year	Population at risk (in millions)
India			
1985	78.4	278,000	354.5
2005	92.2	498,000	539.9
<b>% Increase per annum</b>	<b>0.9%</b>	<b>4.0%</b>	<b>2.6%</b>
Finland			
1985	315.5	39,925	2.531
2005	413.1	54,789	2.652
<b>% increase per annum</b>	<b>2.1%</b>	<b>2.5%</b>	<b>0.3%</b>
<i>* Increase in CIR is seen both in India and affluent countries. The demographic effect is pronounced in India but not in the affluent countries.</i>			

1985<sup>3</sup> to 92.2/100,000 in 2004<sup>1</sup> (Table -3). In terms of the burden of cancer, the increase has been an alarming 79.1% (from 278,000 in 1985 to 498,000 in 2005). The trend in the affluent countries also shows an increase but the demographic effect, which is pronounced in India, is not seen in the affluent countries. In addition, the increasing trend in the affluent countries is a result of earlier diagnosis as is evident from the decline in mortality. In India and all developing countries, locally advanced disease at all sites accounts for more than 60% of the patients seeking treatment, and therefore mortality rates are high. The stage distribution of common cancers in India over the past 3 decades has not shown any significant changes, highlighting the inadequacy of effective cancer control.<sup>4</sup>

### Sex ratio

Registry	Females per 1,000 males	
	Population	Cancer cases
India	942	1,150
More developed regions	1,059	847
Less developed regions	973	887

The sex ratio in the population and in the cancer group indicates that the ratio in India as well as a majority of other developing countries differs from that of the industrialized nations. The male: female (M:F) population ratio in India is 1:0.9<sup>5</sup> whereas in the

cancer population, it is 1:1.15<sup>1</sup>. In the affluent countries, the M:F ratio in the population is equal (1:1.05) and in cancer group, female patients are fewer (1:0.84)<sup>2,6</sup>.

## World pattern of cancer incidence in women

An analysis of the worldwide incidence pattern of the top 5 cancers in women, the CIR, AAR and ranking provides some interesting information.<sup>1,2</sup>

- **Cervical cancer** takes either the top or 2<sup>nd</sup> rank in all developing countries including India, but does not find a place in the top 5 cancers in any of the affluent countries.
- **Breast cancer** finds a place, irrespective of developing or developed countries with variation only in the ranking.
- **Lung cancer** is present in all affluent countries (USA, UK, Japan) and in a large number of developing countries, viz. Philippines, Brazil, Thailand, and Columbia, although with different rankings. Lung cancer does not find a place among the top 5 cancers in women in India.
- **Oral cancer** and cancer of the oesophagus being among the leading cancers is peculiar to India.
- **Colon cancer** occupies the 2<sup>nd</sup> or 3<sup>rd</sup> rank in all the affluent countries but does not find a place in the top 5 in developing countries (Table 5 and 6).

Table 5: Top 5 cancers among women in more developed regions							
US, SEER, White		UK, Oxford		Finland		Japan	
SITE	CIR	SITE	CIR	SITE	CIR	SITE	CIR
Breast	144.9	Breast	128.5	Breast	134.7	Breast	65.7
Lung	59.0	Lung	31.1	Colon	28.2	Stomach	53.9
Colon	39.1	Colon	29.8	Body Uterus	26.7	Colon	48.6
Body Uterus	28.0	Ovary	18.2	Lung	20.7	Lung	29.9
NHL	19.0	Skin Melanoma	17.7	NHL	17.3	Rectum	22.8

*Breast ranked first of all registries; Cervix ranked 13th to 17th behind ovary and body Uterus*

Table 6: Top 5 cancers in less developed regions, 1998 – 2002, female									
Thailand, Chiang Mai		Philippines, Manila		Brazil, Goiania		Malaysia, Sarawak		Pakistan, S. Karachi	
SITE	CIR	SITE	CIR	SITE	CIR	SITE	CIR	SITE	CIR
Cervix	34.2	Breast	38.3	Breast	45.6	Breast	16.6	Breast	37.7
Breast	25.3	Cervix	14.6	Cervix	31.0	Cervix	13.2	Oral Cavity	7.9
Lung	24.6	Thyroid	9.0	Thyroid	9.1	Lung	7.8	Ovary	5.1
Liver	7.3	Lung	8.5	Colon	8.2	Ovary	5.7	Oesophagus	4.2
Ovary	6.2	Ovary	8.4	Lung	7.5	Nasopharynx	5.5	Cervix	4.0

*Cervix ranked 1st or 2nd in all registries; Breast ranked 1st - 3rd in all registries*

## Possible inferences from the world pattern of cancer incidence

- **Cervical cancer** is a disease of the poorer socio-economic countries



- **Breast cancer** occurrence in both developed and developing countries possibly indicates life-style factors in addition to other operative factors.
- **Colon cancer** is possibly related to diet and life-style. The decline in stomach cancer in the affluent countries in the past few decades and its correlation with improved methods of food preservation, consumption of fresh fruits and vegetables etc., are well documented.
- **Lung cancer** is related to tobacco smoking and is universal except in India where the smoking habit in women is low. However, an upward trend in ranking is ominous.
- **Oral cavity cancer** and cancer oesophagus related to tobacco chewing is peculiar to India.

### Changing patterns of cancer incidence in women in India

SITE	CIR
Breast	22.8
Cervix	14.6
Ovary	5.4
Oral Cavity	4.0
Oesophagus	3.6

Uterine cervical cancer occupied the top rank among cancers in women in Chennai and Bangalore in 1984, whereas in Mumbai breast cancer held the top rank. Over the past two decades, there has been a small but progressive decline in the incidence of cervical cancer, along with an increase

in the incidence of breast cancer, both in Chennai and in Bangalore. By 1997, breast cancer came to occupy the leading spot among all cancers in the population in Bangalore, while in Chennai, this occurred in 2002. Today breast cancer is the leading cancer in women in all the demographic registries in India, with cervical cancer occupying the second place.<sup>1,3</sup> A study of the changing trend leading to breast cancer overtaking cervical cancer to occupy the top rank shows that the CIR of cervical cancer in India has reduced from 23.0/100,000 population to 14.4/100,000 between 1984 and 2005, which works out to a 33% reduction. However, the burden of cervical cancer has barely changed from 82,000 in 1985 to 83,000 in 2005. The demographic effect is stronger than the reduction in incidence rates.<sup>1,3</sup> In breast cancer, however, the CIR has increased from 13.9/100,000 population to 22.6/100,000. The increase is 62.5%, with an increase in burden from 49,500 to 122,000 (+146.5%). In this type of cancer there has been a true increase in incidence. However these figures are based on urban registry data only<sup>1, 3</sup> (Table 7).

A study of cervical and breast cancer incidence in the rural registries shows that cervical cancer incidence and ranking is higher than in the urban registries.<sup>1,7</sup> In the case of breast cancer, the reverse is true. In fact, cervical cancer continues to hold the top rank and has not shown any change in the pattern of incidence among women in the rural areas (Table 8).

### **Corollary to rise in breast cancer incidence**

Cancer incidence world over has unambiguously documented that breast cancer incidence is inversely related to cervical cancer incidence and that ovarian and endometrial cancers are directly related to breast cancer

incidence. This is reflected in the rising trends of both endometrial and ovarian cancers in all the urban registries in India.<sup>1,8</sup> This is certainly a matter for concern. Tests for the early detection of breast cancer (in contrast to those for cervical cancer) are expensive. There is at present no accepted method for the early detection of ovarian cancers. Moreover, ovarian cancers are among the most lethal cancers in women.

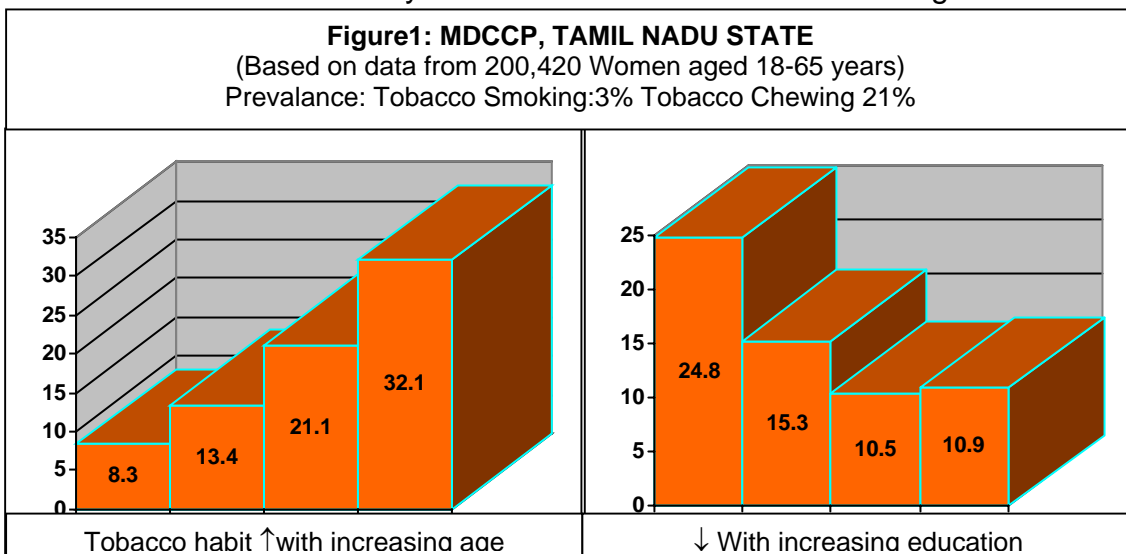
Urban India		Rural India	
SITE	CIR	SITE	CIR
Breast	22.8	Cervix	22.5
Cervix	14.6	Breast	10.3
Ovary	5.4	Oral Cavity	2.6
Oral Cavity	4.0	Oesophagus	2.5
Oesophagus	3.6	Ovary	2.0

*The top 5 cancers constitute 62.8% of all cancers in women in India*

### Oral cancers in women

Oral cancers, a tobacco-related cancer, are a disease found mainly in the lower socio-economic groups and is related to tobacco chewing, snuffing and dipping. Tobacco smoking is low in women. Fortunately oral cavity cancer in women is showing a decline in CIR, from 5.1/100,000 in 1985<sup>3</sup> to 4.5 in 2005<sup>1,9</sup> (Table 9). Our own studies in the Perambalur district in Tamil Nadu highlight the fact that the prevalence of the tobacco habit (other than smoking) in rural women is as high as in the urban areas. It is, however, heartening to note the inverse relationship between the prevalence of the chewing habit in different age groups and the literacy levels. Tobacco use among women is least among the younger age group with an increasing trend with increasing age. It is least in those with education more than >10 years and also shows a decreasing trend with

	CIR
India 1985	5.1
2005	4.5
% decrease per annum	0.6%
Chennai 1985	6.2
2000	5.2
% decrease per annum	5.2



increasing educational levels <sup>10</sup> (Figure 1).

### Socio-economic status (SES) variables in cancers in women

Income and educational levels have been generally accepted as major indicators of SES. CIR in relation to SES variables in the various cancer

Total Incident Cancers: 15,347					
SITE	Crude Incidence Rate per 100,000				
	All education levels together	Illiterate	< 5 years of education	6-12 years of education	>12 years of education
Cervix	23.2	41.7	26.4	14.2	1.9
Breast	25.8	13.8	23.4	29.3	41.0
Oral Cavity	5.5	10.5	5.4	3.3	1.4
Ovary	5.5	3.3	4.2	4.6	6.2
Endometrium	1.9	1.1	1.7	2.2	2.5

sites is significant (Table 10); 74.9% of cervical cancer patients are either illiterate or barely literate, and only 25.1% belong to the mid- or higher educational group. In breast cancer, the statistics are the reverse; with only 14.3% in the illiterate group and 68.3% in the higher educational group<sup>10</sup>. A similar incidence pattern is seen among income levels, categorized as low, mid- and high-income groups. CIR by educational level in the top 5 common cancer sites convincingly confirms the role of SES variables (Table 10).<sup>5,9</sup> Cervix and oral cavity cancers are found predominantly in the lower income/lower educational group, while cancers of the breast, endometrium, and ovary are found more in the higher educational group.

### Special features of cervical and breast cancer in women in India

#### *Cervical cancer*

All the Indian registries document a significantly lower incidence of cervical cancer in Muslim women than in those of other religious groups. The RSI of cervical cancer in Chennai among Hindu women is 21.1, in Christians it is 16.8 and in Muslims it is 9.5 (Table 11).<sup>9,11</sup> This pattern of difference is strikingly marked in respect of penile cancer incidence also. The high incidence of cervical cancer in the Hindu women is attributed to coitus from an early age, and poor penile hygiene in the partner. The low frequency of occurrence of

Registry/ Year/ Site	CIR per 100,000 by religious groups				
	All groups together	Hindu	Muslim	Christian	Others/ Parsi
Chennai (2003-05)					
Cervix	19.6	21.1	9.5	16.8	13.1
Breast	30.6	29.6	34.9	30.0	35.6

cervical cancer among Muslim women is presumed to be due to the practice of ritual circumcision in Muslim male babies, resulting in better penile hygiene in the men<sup>1</sup>.

However, in certain Muslim countries like Indonesia and Malaysia, where cervical cancer incidence in women is documented, penile cancer is also present. In many countries where Muslims predominate, penile cancer is virtually absent (Table 12)<sup>2,11</sup>.

REGISTRY	CIR/100,000	
	CERVIX	PENIS
India, Chennai	24.2	1.5
Malaysia, Sarawak	13.2	0.8
Egypt, Gharbiah	1.5	0.0
Kuwait, Kuwaitis	2.7	0.0
Bahrain, Bahraini	3.9	0.1
Pakistan, South Karachi	4.0	0.0

### **Breast cancer**

The CIR of breast cancer and the cumulative risk in India is significantly lower than in the affluent countries (Table 13). The age distribution of breast cancers, also reflected in the menstrual status, varies considerably in Indian women from that found in the Caucasian races. In India, breast cancer in women <35 years of age constitutes 9-10% of all breast cancers, and women <40 years of age comprise 18-20%<sup>1</sup>. This is 3-fold higher than in the affluent countries where the corresponding figures are just 2 and 8%, respectively<sup>3</sup>. Post-menopausal patients constitute 52-56%, and pre-menopausal patients 45-47% in India<sup>1</sup> whereas the post-menopausal group constitutes 70-75% and the pre-menopausal group 25-29% in the affluent countries<sup>3</sup>. Another feature is the lower oestrogen receptor positivity in Indian women as compared to world data.

	CIR	CUMULATIVE RISK
India	22.6	1 in 21
Affluent countries	114-134	1 in 9-13

### **Other cancers**

Cancers of the cervix, breast and oral cavity (the top 3 cancer sites) constitutes nearly 60% of all cancers in women, other cancers constituting the other 40%. There is an increasing trend in carcinomas of the colorectum, thyroid and lung, together adding up to 9% of all cancers in women (Table 14)<sup>1,3,9</sup>.

Site of Cancer	INDIA <sup>7,3</sup>			CHENNAI <sup>9</sup>		
	1985	2005	% increase per annum	1985	2005	% increase per annum
Colon	1.1	1.8	3.2	0.9	1.8	5.0
Rectum	1.4	2.3	3.2	1.3	2.2	3.5
Thyroid	1.4	2.3	3.2	1.4	3.0	5.7
Lung	1.2	2.5	5.4	0.9	2.6	9.4

## **Risk factors for cancer**

On the basis of geographic variations and epidemiological studies, the International Agency for Research on Cancer has identified major risk factors for cancer. Tobacco in some form accounts for 30% of malignant tumors. Another 30% are related to diet and nutrition, 18% to chronic infections, 1-4% to environmental pollution, and the rest to other factors including alcohol consumption, occupational exposure, certain therapeutic drugs, and hormones. Genetic susceptibility can alter the risk of various types of exposures.

Based on the available documented data, the American Cancer Society and the National Cancer Institution, Bethesda, have provided a dietary guidance for reducing cancer risk:

- reduction of fat intake to less than 30% of calorie intake
- increase in the consumption of fibre-rich foods (cereals) and avoidance of refined foods
- consumption of adequate fresh vegetables and fruits
- minimal consumption of salt-cured, salt-pickled and smoked food
- moderate consumption of alcohol, if at all

Similarly, based on the pattern of incidence of cancers and the Indian experience, our recommendations for risk reduction for common cancers are:

- avoidance of tobacco in any form
- consumption of alcohol, if at all, in moderation
- ensuring a balanced diet; plenty of green vegetables and fruits; avoidance of high-fat foods
- avoidance of obesity
- maintenance of physical hygiene
  - maintaining cleanliness of mouth and teeth
  - avoidance of sharp edges on teeth
  - maintaining genital and sexual hygiene
- avoidance of chronic infections of the oral cavity, chronic ulcers, and chronic pulmonary infection

## **Conclusion**

In conclusion, it would appear, that majority of common cancers in our part of the world are preventable, and risk reduction depends on simple living, personal hygiene, rational habits and a balanced diet. An annual health check-up is essential. Genetic susceptibility, however, will play a significant role in determining the outcome.

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# BIOTECHNOLOGY CAN CONTRIBUTE TO REDUCTION IN THE BURDEN OF MICRONUTRIENT MALNUTRITION IN DEVELOPING COUNTRIES

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*It is indeed a privilege to contribute to this Festschrift or 'celebratory writing' to honour Dr. Gopalan, an eminent nutritional scientist, a formidable medical administrator and leader, and a great son of India. I have had the privilege and the opportunity to know him and to interact with him during the past 25 or more years. Although I have not been blessed with the opportunity to be his direct disciple, in the true traditions of our culture that respects the lineage of teacher and student, I do proudly stake a claim on him as my guru. He is a person with rare intellect, whose grasp of scientific and other issues pertaining to global nutrition are unparalleled, and whose courage and conviction to stand up for matters that affect the developing world are unmatched. His concerns and influence are far wider than the international scientific reputation he has earned over the years. 'The lessons of great men are lost unless they reinforce upon our minds the highest demands which we make upon ourselves - they are lost unless they drive our sluggish wills forward in the direction of their highest ideals'. Dr. Gopalan's lessons will not be lost because many who have known him shall cherish them and soldier on. Those of us who have had the good fortune to know him and to learn from him a truly privileged lot.*

*It was Dr. Gopalan who encouraged and advised me to accept the appointment and move to the London School of Hygiene & Tropical Medicine in the early 1990s. This led to my intellectual journey from nutritional physiology to public health nutrition. My subsequent move to the Food and Agriculture Organization of the UN in Rome contributed further to expanding my horizons and to improving my understanding of the crucial role that agriculture, trade and rural development play in improving the nutrition and health of the populations of developing countries. I have hence felt it appropriate to choose the interesting and much maligned topic of agricultural biotechnology to pay my tribute to him in this Festschrift.*

## **Introduction**

Major advances have occurred in food production and agriculture during the past 30 years in countries like India as a result of the widespread adoption of the benefits of the Green Revolution. The numbers of people who are food-deprived globally has dropped dramatically with the increase in the availability of cereals, although food insecurity is still a major problem in the developing world. The key to these dramatic gains of the Green Revolution is the development and distribution of high-yield seeds and the necessary inputs such as fertilizers and irrigation to make them grow to their full potential. Conventional methods of selective breeding and the crossing of different varieties produced hybrids with desirable characteristics, led to increased productivity and incomes, and brought down the food prices. The Green

Revolution of the latter half of the 20<sup>th</sup> century has led to the Gene Revolution with the recent advances in agricultural biotechnology. Transgenic crop technology is spreading faster than any other agricultural technology; though the furor about 'terminator' genes has died down, controversies about the potential risks of biotechnology persist, such as gene flow (the escape of inserted transgenes into related crops or wild plants), the emergence of resistant pests, and fears that eating genetically modified foods might affect the health of consumers<sup>1</sup>. The U.S. and Canada grow the bulk of transgenic crops—60 percent by area cultivated but developing countries accounted for 38 percent in 2006, almost all of it in Argentina, Brazil, India and China. Transgenic crops have the potential to alleviate some of the concerns we have had with intensive agriculture with regard to the environmental problems and, by further increasing food productivity yet again, they may herald a doubly green revolution<sup>1</sup>.

Micronutrient deficiencies are common in populations that consume largely cereal-based diets lacking in dietary diversity. The poor quality of food and lack of diversity in the habitual diet contributes to deficiencies of micronutrients – a global problem of 'hidden hunger', much bigger than hunger itself – which imposes enormous costs on societies in terms of ill health, lives lost, reduced economic productivity and poor quality of life. There are nearly 2 billion people who suffer nutritional deficiencies of micronutrients such as iron, zinc and vitamin A. While a number of nutritional interventions such as supplementation and food fortification as well as promotion of dietary diversity have been successful to some extent in reducing the problem of micronutrient malnutrition, agricultural biotechnology provides yet another opportunity for sustainable strategies to meet this challenge by developing cereal varieties with not only higher yield potential and yield stability, but also with improved nutritional content<sup>2</sup>. Various conventional approaches and tools of biotechnology are being employed in the development of crop varieties with higher yields and higher content of micronutrients. There are compelling global health and nutritional considerations to persuade plant breeders that micronutrient density traits should be the principal objectives in their work targeted to the developing world. Current evidence strongly supports the contention that there is enough diversity within the genomes of staple plant foods to accomplish this task. Success in doing this would dramatically contribute to improving the health and livelihoods of people in developing countries in a sustainable manner, thereby contributing greatly to furthering national development efforts in these countries.

### **Shifting emphasis from quantity to quality – from yield to nutritional content**

The post-war agricultural revolution commonly referred to as the 'Green Revolution' has been responsible for an extraordinary period of growth in food crop productivity in the developing world over the past 40 years<sup>3</sup>. It brought high-yielding, semi-dwarf wheat and rice varieties, developed through conventional plant breeding methods, to millions of small-scale farmers, initially in Asia and Latin America, but later in Africa as well. The major breakthroughs in yield potential that kick-started the Green Revolution in the



late 1960s came from conventional plant-breeding approaches that initially focused on raising the yield potential of the major cereal crops. For example, yield potential in irrigated wheat has been rising at the rate of 1 percent per year over the past three decades, an increase of around 100 kg/hectare/year<sup>4</sup>. The gains achieved during the early decades of the Green Revolution were extended in the 1980s and 1990s to other crops and to less favoured regions. Essentially, no research or elite germ plasm was available for many of the crops grown by poor farmers in less favourable agro-ecological zones (such as sorghum, millet, barley, cassava and pulses) during the early decades of the Green Revolution, but since the 1980s modern varieties have been developed for these crops and their yield potential has risen<sup>5</sup>. In addition to the continuing progress in the yield of cereal crops, conventional plant breeders continue to have successes in many related fields. These include the development of crops with durable resistance to a wide spectrum of insect pests and diseases, plants that are better able to tolerate a variety of physical stresses such as drought and salinity, and crops that require a significantly lower number of days of cultivation. All these developments basically contribute to increases in quantity of cereal grain or crop yield globally. However, in recent years this emphasis on quantity has shifted, and increasing efforts are being made to enhance the taste and nutritional qualities of cereal grains.

The approaches to improving the quality of food crops have varied from those focused mostly on methods that are biotechnology-driven and resort to the use of transgenics, to those that have relied almost entirely on classical plant breeding techniques. The former is more recent and driven by science and the private sector, while the latter has a long history with varieties chosen by the small farmer for their special characteristics and have contributed much to the preservation of plant diversity in the world. Increasingly, there has emerged a hybrid method, with biotechnology contributing to the identification of desirable qualitative traits (using markers), which are then bred by classical methods. This last approach has enormous potential, because it sidesteps the issues related to safety (both with regard to health and environmental concerns). It also has the added advantage that it enables the combination of characteristics that have been hitherto favoured for the purpose of increasing yield i.e. quantitative traits, while at the same time addressing the need for better nutritional and related characteristics, i.e. qualitative traits.

### **The problem**

The Green Revolution followed by the recent advances in crop sciences have contributed to increasing crop yields, and thus to the availability of food to tackle the problem of global hunger. Hunger worldwide is now estimated to affect over 854 million people, most of them (820 million) in the developing world<sup>6</sup>. However, the global problem of micronutrient deficiencies is much bigger than hunger, and is hence referred to as 'hidden hunger'. Micronutrients – vitamins, minerals and trace elements– are essential chemical compounds that are present in small amounts in food and fulfill many important functions. These nutrient deficiencies impose enormous costs

on society in terms of ill health, lives lost, reduced economic productivity and poor quality of life.

Globally, the prevalence of vitamin and mineral deficiencies is remarkably high (Table 1), and it is estimated that one-third of the world's people do not attain their physical and intellectual potential because of micronutrient deficiencies (Micronutrient Initiative & UNICEF, 2004). Estimates based on data from more than 80 countries in the developing world indicate that iodine deficiency disorders (IDD) in pregnancy cause almost 18 million babies a year to be born mentally impaired, and IDD is estimated to lower the intellectual capacity of people in almost all the nations reviewed by this report by as much as 10-15%, while iron deficiency at the age of 6-24 months is impairing the mental development of 40- 60% of the developing world's children. Severe iron deficiency anemia (IDA) is responsible for the deaths of more than 60,000 young women a year in pregnancy and childbirth, while iron deficiency in adults is estimated to contribute to productivity losses of up to 2% of the GDP of these nations. Vitamin A deficiency (VAD) on the other hand, compromises the immune status of approximately 40% of the developing world's under-5-year-old children and is the cause of approximately 1 million deaths of young children each year. It is important also to recognise that the prevalence of multiple (two or more) deficiencies occurs in 50% of the children in whom any deficiency is present, and this adds to the immeasurable burden on individuals, health and social services, education systems and families. Further, it is becoming apparent that other micronutrient deficiencies like zinc and folate deficiency are widespread enough to be considered as being of sufficient public health importance in view of both health and associated economic consequences. The economic and social costs of 'hidden hunger' can be fathomed only by recognizing that micronutrient deficiencies affect cognitive and physical development and decrease school performance in children, compromise work output, productivity and earning capacity of adults, impair immunity and increase susceptibility to infectious diseases, and increase mortality, particularly among vulnerable groups such as pregnant women and children.

<b>Table 1: Estimated global impact of micronutrient malnutrition</b>	
Micronutrient Deficiency	Estimated impact
Vitamin A deficiency	140 million pre-school children affected with VAD <sup>1</sup> Contributes to 1.15 million deaths in children every year <sup>2</sup> 4.4 million children suffer from xerophthalmia <sup>1</sup> 6.2 million women suffer from xerophthalmia <sup>1</sup>
Iron Deficiency	2.0 billion women (96 million of them pregnant) <sup>2</sup> 67,500 maternal deaths per year from severe anaemia <sup>2</sup>
Iodine deficiency	1.98 billion at risk with insufficient or low iodine intakes <sup>3</sup> 15.8% of population worldwide have goitre <sup>3</sup> 17.6 million infants born mentally impaired every year <sup>2</sup>
Folate deficiency	Responsible for 200,000 severe birth defects every year <sup>2</sup>
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More than two billion people in developing countries are victims of this insidious form of hunger due to the poor quality of food and lack of diversity in the habitual diet. Deficiencies of micronutrients are common in populations that consume largely cereal-based monotonous diets. Cereals do not contain carotenoid compounds (precursors to vitamin A) in the grain. Consequently, VAD often occurs where the diet is monotonous and relies heavily on only cereal staples. The amount of bioavailable iron is dependent on the content and source of iron in the diet and on iron absorption during the digestive process. The absorption of dietary iron of vegetable origin is relatively low, and this is considered to be a major factor in the causation of iron-deficiency anaemia. Also, cereals are high in phytic acid, which is a potent inhibitor of iron absorption. Foods that enhance non-haem iron absorption such as fruits and vegetables rich in ascorbic acid are often not consumed in adequate amounts in developing countries. Haem iron, which is relatively well absorbed by the human intestine, is found primarily in animal products such as meat. Often, animal source foods are limited in most diets in developing countries, because of high cost and limited availability. IDA is exacerbated since haem iron-rich foods are often a negligible part of a typical diet in a developing country.

### **The solutions**

Strategies to combat micronutrient deficiencies are probably among the most cost-effective of all health interventions. The World Bank<sup>7</sup> estimated that deficiencies of the three major micronutrients i.e. Vitamin A, iodine, and iron alone could contribute to reducing as much as 5 percent of gross domestic product (GDP) in developing countries, whereas the cost of addressing these deficiencies comprehensively and sustainably would cost less than one-third of a percent of GDP. The World Health Organisation<sup>8</sup> estimated that, while 3.7 million deaths per year in children are attributable to underweight, deficiencies of vitamin A, iron and zinc each caused an additional 750,000 – 850,000 deaths. Effective nutritional interventions, including breastfeeding, complementary feeding and micronutrient supplementation, can reduce child mortality significantly and save 2.4 million children's lives each year.

### ***Nutritional interventions***

The time-tested strategies universally promoted have hitherto focused on nutrient supplementation and fortification with micronutrients of commonly consumed foods. Supplementation and fortification however, only address the symptoms and not the underlying causes of micronutrient deficiencies. Other complementary interventions include the treatment of parasitic infestations, which very often are important contributors to micronutrient deficiencies such as that of iron. The alternative is to advocate and support sustainable interventions that alter behaviour, such as nutrition education and the promotion of dietary diversity and investments in home vegetable gardens, which will contribute to dietary diversification. While these strategies have been tried with varying degrees of success and continue to play an important role in addressing the immediate needs of vulnerable segments of the population (e.g. supplementation of infants and children alongside universal

immunization programmes or the provision of micronutrient supplements to pregnant women) increasingly more emphasis is being placed by international agencies on food fortification strategies<sup>9</sup> since they can be categorized as food-based approaches and hence probably sustainable in the long term.

### ***Agricultural biotechnology solutions***

It is obvious that improving and enhancing the nutritional quality of cereal grains by increasing their micronutrient content would be a sustainable and more effective approach, given that a major proportion of the diet of vulnerable populations in the developing world are cereal-based. For example, rice alone contributes to 23% of the calories consumed worldwide, and countries that rely on rice as the main staple often consume up to 60% of their daily calories from this cereal<sup>10</sup>. The International Conference on Nutrition (ICN) Declaration<sup>11</sup> had advocated a strategy to combat 'hidden hunger' that stated: "Ensure that sustainable food-based strategies are given first priority, particularly for populations deficient in vitamin A and iron, favouring locally available foods and taking into account local food habits." Supplementation was to be progressively phased out as soon as micronutrient-rich food-based strategies enabled adequate consumption of micronutrients. It has been pointed out that a sustainable solution to the problem of malnutrition can come only when it becomes possible to improve the content of the missing micronutrients in the major staple crops<sup>12</sup>

In agriculture, biotechnology- or molecular biology-based approaches are used primarily in one of two ways:

- genetic engineering to create transgenics or genetically modified organisms (GMO) by manipulating, deleting or inserting genes in order to change the organism; and
- marker-assisted selection to speed up conventional crop and animal breeding. Both can and have played a role in providing biotechnology-based solutions to improve the nutritional quality of agricultural products.

### ***Genetic engineering***

The production of "Golden Rice" was a major event in the use of genetic engineering to deal with the problem of addressing food security for developing countries from a qualitative perspective, given that the major forms of micronutrient malnutrition are "iron, iodine and vitamin A deficiency". In addition to the range of nutritional interventions hitherto promoted, biotechnology using genetic engineering provided a window of opportunity to tackle this global problem in a more sustainable manner by altering the nutritional quality of staple crops that constitute the bulk of the staple diet in developing countries. Using the example of rice, the necessary genes for improving the availability of carotenoids (vitamin A precursors) are not available in the rice gene pool; hence genetic engineering was an approach that was potentially very attractive. Since rice endosperm does not contain any provitamin A, the initial objective was to introduce the entire biochemical pathway for its synthesis. Several years of research culminated in the production of 'Golden Rice' by a group of Swiss transgenics researchers

working with daffodil genes. The endosperm of Golden Rice contained substantially higher levels of provitamin A, visible as "golden" colour of different intensities in different lines<sup>13, 14</sup>. The best provitamin A line had 85% of its carotenoids as beta-carotene. Other lines had less beta-carotene, but high levels of lutein and zeaxanthin, both of which are of nutritional importance because they have other positive nutritional effects<sup>13</sup>. The first-generation Golden Rice, with a gene from daffodil and a common soil bacterium, drew considerable criticism as a technological solution to a problem associated with poverty and hunger. It was argued that Golden Rice would encourage people to rely on a single food rather than the promotion of dietary diversification. Detractors also noted that a normal serving of Golden Rice contained only a small fraction of the recommended daily allowance (RDA) of beta-carotene<sup>1</sup>. Golden Rice 2 was developed by replacing the daffodil gene with an equivalent gene from maize. This modification increased the amount of beta-carotene approximately 20-fold, so that ~ 140 grams of the rice would provide a child's RDA for beta-carotene.

Another approach with similar objectives was to increase the availability of iron while reducing the inhibitor content or adding a resorption-enhancing factor. Only 5% of the iron in the rice plant is in the seed and hence an attempt was made to create a sink for iron storage within the endosperm by expressing a ferritin gene from *Phaseolus*, resulting in a 2.5-fold increase in endosperm iron content. Feeding studies with peptides from muscle tissue had shown that cystein-rich polypeptides enhance iron resorption. A metallothionin-like gene from *Oryza* achieved a 7-fold increase in endosperm cystein<sup>15</sup>. Since interference with the phosphate storage could affect germination, expression of the phytase gene had to be achieved in such a manner as not to interfere with germination. The enzyme was therefore excreted into the extra-cellular space, and one transgenic line that was developed expressed the phytase to levels 700-fold higher than endogenous phytase. However, the transgenic enzyme in this line did not refold properly after cooking; it had lost its thermo tolerance and was hence ineffective. New transgenic plants are being developed, aimed at targeting the enzyme to phytase storage vesicles so as to reduce the phytate content directly and thereby overcome the loss of enzyme during cooking. These three genes that influence iron availability and absorption are being combined with the provitamin A genes by crossing.<sup>15</sup> It is now well recognised that vitamin A-deficiency indirectly interferes with iron resorption, since higher intakes of beta-carotene (converted to retinol after ingestion) may promote absorption of iron and vice versa. The FAO, along with its partner in IAEA as well as other investigators, have approached this problem differently. Their aim is to induce mutations using nuclear techniques<sup>16</sup> to produce strains of cereals with higher yields of micronutrients or low phytic acid content, thereby improving the bioavailability of these nutrients in cereals. Raboy<sup>17</sup> has developed low phytic acid (or lpa) mutant varieties of maize, rice and barley using similar techniques. The phytic acid content of lpa seeds is reduced by 50-80 percent as compared to non-mutant seeds. The total amount of phosphorus remains the same; phytic acid is replaced with inorganic phosphorus, which does not bind a range of trace minerals, thus making the nutrients available for absorption.

### Marker-assisted selection and breeding

<b>Table 2: Genetic variation in concentrations of iron, zinc, beta-carotene, and ascorbic acid found in germplasm of five staples, (mg/kg of dry weight)<sup>4</sup></b>				
	Iron Conc. (mg/kg)	Zinc Conc. (mg/kg)	Beta-carotene *** (mg/kg)	Ascorbic Acid (mg/kg)
Rice, brown	6-25	14-59	0-1	-
milled	1-14	14-38		-
Cassava: root	4-76	3-38	1-24*	0-380*
Cassava: leaves	39-236	15-109	180-960*	17-4200*
Bean	34-111***	21-54	0	-
Maize	10-63	12-58	0-10	-
Wheat	10-99**	8-177**	0-20	-
Notes: * fresh weight basis; ** including wild relatives, *** range for total carotenoids is much greater.				
<sup>4</sup> Source: International Center for Tropical Agriculture, 2002.				

A careful examination of the composition of nutrients in a variety of crops demonstrates a wide genetic variation in the nutrient content of a range of food crops such as rice, cassava, beans and maize (Table 2) which contribute to the vast biodiversity in the plant kingdom. A similarly wide range in the micronutrient content of a single staple such as rice (Table 3) is also evident among the varieties of rice grown throughout the world (Kennedy & Burlingame, 2003). Conventional plant breeding has not only demonstrated the existence of substantial and useful genetic variation that exists in the germ plasm of key crops, but also that it can be a valuable means by which varieties can be chosen and cross-bred to improve and enhance their nutrient content. Since plant breeding takes a long time, using molecular biological markers to identify traits can speed up the process. This approach, while falling under the broad rubric of agricultural biotechnology, is distinct from genetic engineering in that it involves looking at genes and not modifying or changing them. In this case, molecular biology is aiding the process of plant breeding by speeding up the identification of varieties with special characteristics with the assistance of markers, thus ensuring the outcomes of crossing different strains.

A strategy of breeding plants that enrich themselves and load high amounts of minerals and vitamins into their edible parts has the potential to substantially reduce the recurrent costs associated with fortification and supplementation. But this will be successful only if farmers are willing to adopt such varieties, if the edible parts of these varieties are palatable and acceptable to consumers, and if the incorporated micronutrients can be absorbed by the human body<sup>18</sup>. According to Bouis, if a plant breeding strategy to combat micronutrient deficiency is to work and be universally adopted, particularly in developing countries, five crucial questions need to be first addressed. They are:

- Is it scientifically feasible to breed micronutrient-dense staple food varieties?
- What are the effects on plant yields and will farmers adopt such varieties?

- Will micronutrient-density change the characteristics of the food that are important to consumers?
- Will the extra micronutrients in staple foods be bioavailable to humans?
- Are there other cheaper or more easily sustainable strategies for reducing micronutrient malnutrition?

Nutrient	Range	Average	Highest nutrient content	Lowest nutrient content
Protein (n=1339)	5.55 – 14.58 g/100g	8.55	Indica CR1707 (Costa Rica)	Indica Rd 19 (Thailand)
Iron (n=95)	0.70 – 6.35 mg/100g	2.28	Long grained <sup>a</sup> red (China)	Undermilled Red <sup>a</sup> (Philippines)
Zinc (n=57)	0.79 – 5.89 mg/100g	3.34	Ganjay Roozy (IRRI)	Long grain <sup>a</sup> Fragrant (China)
Calcium (n=57)	1.0 – 65.0 mg/100g	26	ADT-21, red (India)	Brown Japonica <sup>a</sup> (Korea)
Thiamin (n=79)	0.117 – 1.74 mg/100g	0.475	Juchitan A-74 (Mexico)	Glutinous rice <sup>a</sup> special grade (China)
Riboflavin (n=80)	0.011 - 0.448 mg/100g	0.091	Tapol Dark Purple (Philippines)	Mun-pu red (Thailand)
Niacin (n=30)	1.97 – 9.22 mg/100g	5.32	Long grained <sup>a</sup> purple (China)	Glutinous round <sup>a</sup> grained (China)
<sup>a</sup> These data come from Food Composition Tables, and do not strictly represent rice varieties Source: Kennedy and Borlingame, 2000				

Thus the ICN goal of promoting sustainable ‘food-based strategies’ to enable adequate consumption of micronutrients in the developing world can be achieved by the introduction of ‘bio-fortified’ crops, which are varieties bred for their qualitative aspects and not merely to improve yields. The feasibility of plant breeding approaches for improving the micronutrient content of staple crops is real<sup>19</sup>. This is an approach that uses both classical plant breeding and modern biotechnology. Breeding programmes can readily manage nutritional quality traits, which, for some crops, are highly heritable, simple to screen, and offer the possibility of increasing the content of several micronutrients in the same variety. The desirable traits are sufficiently stable across a wide range of growing environments. In addition, these traits for quality and high nutrient content can be combined with the traits for which staples are specifically bred i.e., superior agronomic characteristics and high yields. Biotechnology, on the other hand, offers a repertoire of techniques, in particular the use of marker techniques, which will help scientists to better understand and identify the genes responsible for high nutrient content help to the identification of the relevant markers will enable marker-assisted selection to facilitate transfer of these desirable traits through conventional plant breeding.

There is considerable progress in this new area of biofortification, and the good examples are iron-rich rice (International Rice Research Institute, Philippines), quality-protein maize (International Maize & Wheat Improvement

Centre, Mexico), high-carotene sweet potato (International Potato center, Peru), and high-carotene cassava (International Center for Tropical agriculture, Colombia)<sup>20</sup>. The major advantage of the 'biofortification' approach is that this strategy does not depend on the change in behavior of either the producer (farmer) or the consumer. Already existing high-yielding varieties can be used, which are being widely cultivated and consumed. The increase in nutrient content is a natural variation, and hence breeding specifically for these qualities need not necessarily alter appearance, taste, texture or cooking qualities, thereby having no impact on consumer behaviour. Combining nutritional quality traits with those for high yield or pest- or drought-resistance ensures ready adoption by the farmer, and market success. An added advantage is the increasing recognition that high levels of trace minerals in seeds also aid plant nutrition and may thus contribute to better growth and yields of staple crops. Because trace minerals are important not only for human nutrition but also for plant and animal nutrition, plant breeding has great promise for making a significant, low-cost, sustainable contribution to reducing micronutrient deficiencies even among livestock and other agricultural food products<sup>22</sup>. It may thus have other important spin-off effects for environmentally beneficial increases in farm productivity in developing countries and may thereby contribute to agricultural trade from the South.

### ***Cost-benefits of agricultural biotechnological approaches***

The World Bank<sup>7</sup> estimates that, at the levels of micronutrient malnutrition existing in South Asia, 5 % of gross national product is lost each year due to deficiencies of just three nutrients: iron, vitamin A and iodine. In a hypothetical country of 50 million persons burdened with this rate of malnutrition, deficiencies in these three nutrients could be eliminated through fortification programmes costing a total of US \$25 million annually, or 50 cents per person per year. The monetary benefit of this \$25 million investment is quite high in terms of increased productivity - estimated at \$20 per person per year, or a 40-fold return on an investment of 50 cents. These benchmark numbers will be used later in this paper as a basis of comparison with the benefits of a plant breeding strategy. A calculation of benefit–cost ratios for biofortification plant breeding has been made by Bouis<sup>22</sup>. Expressed in present values, the costs are ~ US \$13 million and the benefits are ~ \$274 million, giving a benefit-cost ratio of over 20, which is quite favourable despite the very conservative assumptions made, and despite the long time-lag between investments and benefits. This last point highlights an essential difference between investments in standard fortification programmes and biofortification through plant breeding strategies. Standard fortification programs must be sustained at the same level of funding year after year. If investments are not sustained, benefits disappear. Such investments apply to a single geographical area, such as a nation-state. By contrast, research investments in plant breeding have multiplicative benefits that may accrue to a number of countries. Moreover, these benefits are sustainable since, as long as an effective domestic agricultural research infrastructure is maintained, breeding advances typically do not disappear after initial investments<sup>23</sup>.



## **Improvements in other qualities of food that may benefit agricultural trade from developing countries**

Qualities of food other than its nutrient content are also traits that producers, marketers and consumers look for. While producers and marketers favour traits that ensure long shelf-life, appearance and safety of products, consumers also go for the organo-leptic qualities like taste, texture and cooking characteristics. Biotechnology offers the potential to enhance and select for several positive qualities of agricultural products that consumers look for and thus promote agricultural trade. A survey of the biotechnology-related activities in this area that are already in progress in different regions in the world indicates that wide ranges of problems are being tackled. These include improving shelf-life and appearance of fruits, vegetables and flowers. Examples are papaya (shelf life), tomato (appearance and shelf life by delayed and improved ripening), potatoes (by increasing starch content and enhanced bruise resistance); orchids (by improved colour and shelf life); palm oil (improved quality); oil seeds (improvement in fatty acid composition - high lauric acid in rapeseed, high oleic acid in soya); cocoa (improved butter content and flavour); cassava (change in starch quality); and soybeans (stripping of allergenic genes). Other areas in which biotechnology is playing an important role are: reduction of toxicants (linamarin in lima beans, lotaustralin in chick peas, solanine in potatoes, and cyanogenic glycosides in cassava); reduction of anti-nutritional factors (lectins and protease inhibitors); enhancing health promoting substances i.e. phytochemicals like lutein in tomatoes; and even foods like bananas and potatoes being engineered for pharmaceutical products or for vaccines against infections, as recently reported<sup>24</sup>.

## **Conclusions**

A sustainable approach to reducing micronutrient malnutrition among vulnerable populations in developing countries is to enrich major staple food crops with micronutrients through plant-breeding strategies assisted by biotechnology, offering direct and indirect benefits to producers and consumers in developing countries<sup>23</sup>. Investment in breeding nutrient-dense staple foods can make a major contribution to reducing micronutrient deficiencies, and at the same time address the global problem of hunger. Because of the inherently wide variation in the micronutrient content of the available staple crops and the inherent compatibility of high yields and trace mineral density, success in increasing the mineral content of staples can be achieved in the short-run through conventional plant-breeding techniques. Plant breeding is a new strategy for improving nutrition, and it is essential to make these early, nutritionally improved varieties available to farmers for commercial production. Furthermore, doing so would also improve crop productivity. When micronutrient-dense seeds and grains are planted in micronutrient-poor soils, the farmer adopts the micronutrient-enriched seeds once they are developed. Any resulting improvements in micronutrient status must be measured to demonstrate the feasibility and practicality of plant breeding for improving micronutrient nutrition<sup>25</sup>. The time has come to invest in agricultural technologies to find sustainable solutions to micronutrient

malnutrition. Plant breeding is one such technology that should be adopted by the world's agricultural community and should be supported by the world's nutrition and health communities.

In summary, biotechnology not only offers the opportunity to increase crop yields and thereby increase the availability of food (quantity), but also has the enormous potential to improve the quality of staple foods and thus contribute to better nutrition of populations. The production of "golden rice" was a major event in the use of biotechnology to address the problem of micronutrient malnutrition by bringing about a qualitative improvement in the nutrient content of a cereal. Sustainable solutions can come only when it is possible to improve the content of the missing micronutrients in the major staple crops. Promoting sustainable 'food-based strategies' to enable adequate consumption of micronutrients can thus be achieved by the introduction of 'bio-fortified' crops which are varieties bred for their qualitative aspects and not merely to improve yields. The feasibility of plant breeding approaches worldwide for improving the micronutrient content of staple crops is real. This is an approach that uses both classical plant breeding and modern biotechnology. Plant breeding has already demonstrated the existence of substantial and useful genetic variation that exists in the germ plasm of key crops. Breeding programmes can readily manage nutritional quality traits, which for some crops are highly heritable, simple by screening, with the possibility of increasing the content of several micronutrients in the same variety. The desirable traits are sufficiently stable across a wide range of growing environments and, in addition, these traits for quality and high nutrient content can be combined with the traits for which staples are specifically bred, i.e. superior agronomic characteristics and high yields. Biotechnology offers a repertoire of techniques and helps in the identification of the genes responsible for high nutrient content, thereby making marker-assisted selection possible. This approach will facilitate transfer of these desirable traits through conventional plant breeding. However, nutrient content is not the only trait producers and consumers look for in a globalised world of increasing agricultural trade. While producers and marketers would favour traits that ensure long shelf-life, appearance and safety of products, consumers also go for the organo-leptic qualities like taste, texture and cooking characteristics. Biotechnology offers the potential to enhance and select for several other positive qualities of agricultural products. Given the importance of agricultural trade for developing countries, the judicious use of biotechnology may further the economic development of the developing countries while helping to tackle the problem of malnutrition in their midst.

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# FOOD AND NUTRITION CURRICULUM IN HIGHER EDUCATION IN HOME SCIENCE FOR CHANGING INDIAN SOCIETY

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## Introduction

Home Science education stands on a tripod: sensitization to the sciences, to technology, and to the social sciences. It explores the use of meaningful scientific research in improving the quality of life of people at large and of vulnerable groups in particular. It endeavours to impart value-based education to students. Perhaps for this reason, there is a lot of variation within the country with respect to home science education, depending on local needs. The following piece of thought is for all those who want to bring to reality what Home Science education particularly in Food and Nutrition has the potential to achieve. The purpose of the mission of teaching Food and Nutrition in Home Science Colleges and Departments is two-fold. First, to enlighten the students as to the changing dietary and lifestyle needs of communities in health and disease; and second, to teach them to apply this knowledge in promoting health in partnership with government, industry, institutions and the community.

Community counselling is a major focus of our education and we teach these skills to our students. Our communication techniques have advanced from posters and flip books to more technology-savvy video films, CD Roms, multimedia presentations and CAL modules. Every student of Nutrition studies Food Science, diets throughout the life cycle, dietetics, and community nutrition, apart from acquiring a working knowledge in the areas of child welfare, communication, physiology, microbiology, biochemistry, and social sciences including economics and sociology. Today our students have to be sensitized to examining issues related to:

- impact and efficiency of government programmes
- food insecurity and human rights
- nutrition insecurity: micronutrient deficiencies
- global markets and health foods
- nutritional economics
- nutritional transition
- information technology & computer application in home science
- innovative methods of counselling using state-of-the-art media systems
- latest techniques for research and evaluation
- community skill enhancement
- basic research: food safety, tolerance limits, nutrigenomics, functional foods, ergonomics, etc

## Issues and concerns

### ***Impact and efficiency of government programmes***

We have been involved in the planning, implementation and evaluation of many government programmes. Severe malnutrition and frank deficiencies

are not seen any more. Large population disaster management is better. There is also adequacy of food grains in spite of rapid population growth. Infant mortality in the under-5 age group has drastically reduced. But there are many pending issues. We are still struggling to reach the unreached. We are still not able to reach the under-2 age group, even within the so-called reachable societies. Newer problems have emerged. Several multifactorial nutritional problems have surfaced. Urbanization has led to an increase in the slum population. Studies have shown that the living conditions in urban slums are more deleterious to health than the living conditions of the rural poor. There are many more social abuses seen among slum dwellers, making the vulnerable even more vulnerable. Targeting these communities for nutrition and health education will help them to optimize their resources, making them aware of available government initiatives and encouraging them to access it. We should identify lacunae and reasons for lack of penetration. More effort is needed to work towards successful implementation of development programmes. If the communities that need the facilities do not avail them, they are lost by pilferage, resulting in failure of government initiatives.

A Home Scientist must

- sensitize families to 'wake up' and access government programmes
- sensitize families to optimize their resources
- sensitize families to work towards attaining long-term good health
- ensure local capacity-building to make the initiatives sustainable

### ***Food insecurity and Human rights***

In the past we have seen efficient disaster management of large populations during the drought of 1984 and the Bhuj earthquake. But now there are many distressing incidences of avoidable deaths. In spite of adequate buffer stocks with the Food Corporation of India certain pockets of the population remained unreached. The foodgrains held by the FCI are not efficiently stored. There is a general rise in the prices of food and fuel, and generally in the cost of living. Surely a larger number of people are food insecure today. It is true that in a large heterogenous country such as ours adverse events are bound to happen; but people of this country, wherever they may live, have the right to be reached in times of need - be it need for medical care, shelter or food. Illiteracy, lack of potable water and lack of hygiene are issues that continue to undermine efforts at human development, and tackling them calls for major government initiatives and public will. The rate at which basic facilities reach communities is slow, and the goal is distant.

Our students should evolve innovative programmes for community participation in a Hunger-Free India movement. We should make it a part of our curriculum and encourage students to work in this area as field projects. For poor and BPL families, the PDS is not sufficient. More imaginative, newer approaches should evolve so as to quicken the pace of ensuring food security in the country. Having short-term operations such as feeding programmes were valid 20-30 years ago, but they should not impede implementation of long-term approaches. The goals will take longer to achieve if long-term

approaches are not given impetus. We must encourage our students to think along these lines. They should be sensitive to legal and social issues such as the right to food, child rights and gender issues.

### ***Nutrition insecurity***

The insufficiency of essential micronutrients in the diet is referred to as “hidden hunger”. Some nutrients that are extremely important for health, such as iron, vitamin A, iodine, and probably zinc, are still not adequately met through diet alone, especially among the vulnerable groups, in spite of sufficiency of food. Thus, even where there is food security, there is often nutrition insecurity. Our students work extensively in mapping the extent of deficiencies in community diets, and the role of supplements. The Tenth Five-Year Plan (2002-2007) envisaged covering more adolescents, school dropouts, and pregnant and lactating mothers under the IFA programme. It also recommended a study of consumption of iodized salt by various communities. The promotion of vitamin A adequacy by dietary diversification is another important strategy.

Our students should be academically equipped at all levels understanding the needs of the community, advocacy, and ability to clarify doubts, thereby helping to achieve national goals. In my judgment they are 80% equipped already. More inputs are necessary to sharpen the skills of the students in carrying out sampling and statistical design professionally and competently. Programme planning and evaluation should be an important component of the curriculum for students of Nutrition.

### ***Global Markets and Health Foods***

In the context of the WTO, emerging global markets and global pressure, it will be imperative to ensure the quality of dietary inputs. This will make things expensive and impact the deprived communities. Teaching entrepreneurial skills for setting up of small-scale industries will become a bigger challenge. These approaches will not ensure sustainable development in the process of empowerment. We have to train our students in the food industry, catering industry, and dietetics to understand and achieve international standards. They should be knowledgeable about how to handle issues of pesticide residue, GM foods, patents and consumer protection. They should become competent to deal with issues such as food safety, genetic modification of foods, food labeling, trans-fatty acid restrictions, food fortification, nutraceuticals, functional foods, health foods, etc, to name just a few.

### ***Nutrition economist***

There have been very few eminent scholars outside the field of Nutrition who have written on the economics of malnutrition, natural disasters and food security, the economics of government programmes, definition of the poverty line, etc. A country the size of our needs more qualified personnel to work in this area. Efforts should be made for interdisciplinary education of students of various fields. For instance, those who are majoring in Nutrition should be

taught economics and social medicine. This will help in major capacity building of our professionals, whether they be nutritionists, medical personnel or economists.

### ***Nutritional transition***

There is a global epidemic of obesity. In India we have the added burden of a high incidence of diabetes. Many sections of the population in India have experienced sudden affluence, and this has catapulted many malnourished subjects into obesity and insulin resistance, due to syndrome X. In other words, the malnourished subjects attained obesity before they could attain good health! We still have a high percentage of low birth weight (LBW) infants. When these infants are well fed, they are more likely to develop obesity and diabetes in later life than are normo-weight infants. In one of my recent studies on dietary and lifestyle practices of young executives in multinational companies, 11% were already suffering from one or more diseases, 10% had hypertension, and up to 53% were overweight or obese. Stress and lack of exercise were major precipitating factors for these diseases, with hardworking young executives wanting to meet targets in a market that is in recession. There is no job stability, and working hours are abusive. They have meals in the office canteen; there is an increase in the frequency of eating out, and also an increase in alcohol and tobacco consumption. These executives do not make healthy food choices, and their diets have high levels of energy, protein, simple sugars, fats and cholesterol. Their dietary fiber consumption is low due to limited consumption of vegetables and fruits. This phenomenon has now invaded the classrooms, with the incidence of obesity and hypertension rising among school children because of the stress of examinations, low levels of physical activity, and long hours of study extending late into the night.

Our students should be able to discern some of these transitions. They should be exposed to innovative counselling modules. For example, in our study we gave counselling based on body composition data, which was more authentic and convincing. The HR managers of the MNCs were told to encourage their staff to go for walks and use the stairs. The canteen managers of MNCs can be counselled and can be encouraged to prepare low-fat meals. The companies were encouraged to set up a gym or active recreation room. These newer approaches should be handled by our students independently and professionally.

The school health program needs urgent attention to prevent early onset of lifestyle diseases. Children should be encouraged to participate in physical activity and games. But mere encouragement is not enough. Today we need comprehensive BCC behavior change strategies.

### ***Information technology and computer applications in home science***

Almost 35% of India's population is obese. A large number of these people are educated, and yet have faulty dietary and lifestyle practices. Some of these educated people can be reached through the media, especially through the internet, CAL module, etc. Several Ministries of the Government of India,

including the Ministry of Women and Child Development, have websites to reach lower income groups, ANW workers, etc. The internet now has considerable penetration into large sections of the community and is a potent tool.

Our students should be able use the computer in counselling, database creation and nutrient analysis, and for opening portals to the treasure-house of information that is available on the Web. Such inputs will increase their value in job markets and equip them with skills to meet the changing needs of India. Our curriculum should adequately meet this objective.

### ***Innovative methods of counseling using state-of-the-art media systems***

Apart from computers, other media avenues can also be used. The use of community radio for advertisements and jingles can supplement traditional methods of one-to-one or door-to-door reach; we should also use more imaginatively the print media, panchayati raj institutions, and school- and college-based institutions. Our students should clearly understand social and government structures, be able to apply for the necessary permissions, and encourage community participation when working towards social change. They should be able to innovatively write radio or video scripts targeted towards specific, sensitively selected target populations.

### ***Latest techniques in research and evaluation***

The estimation of trace elements requires sophisticated techniques such as atomic absorption spectro-photometer and inductively coupled plasma mass spectrometer. The analysis of pesticides, food flavours, food additives, and fatty acids needs GLC and HPLC. Can we sit back and wait for someone else to do the estimations needed for our research and evaluation studies? How can one estimate the efficacy of IFA supplementation if folate, homocysteine etc. cannot be estimated? Ferritin is estimated on the principle of radio-immuno assay and several other nutrients require the study of radioisotope turn over. These techniques are now basic techniques in the field of Nutrition. All the students need to be trained in these basic techniques. Placement and internship done nationally and internationally are now becoming increasingly important.

Further, research designs for large populations need better understanding of statistical concepts such as odds ratio, cohort studies, and multiple regression analysis. Students should study and use more and more of such designs in order to increase their effectiveness in community work. We can involve ourselves in larger teams to do multi-centric studies so as to have larger databases from which to derive normatives. Competencies in all types of statistical packages are imperative.

### ***Community skill enhancement***

We teach and empower our students with skills necessary for entrepreneurs and to impart knowledge to enhance the quality of life. The students should have adequate skills in marketing and quality assurance for food product



development, home catering, dietetic practice, community participation programmes and the development of cutting-edge technologies. They should be taught entrepreneurship and how to take a product to scale, within the boundaries of government laws.

In our curriculum, the students would have several field placements, which will help them to understand the community's needs and abilities. They should empower the communities by forming self-help groups to start income-generating activities. The skills, which they impart in the community, should be in keeping with excellence in product quality, sustainability and marketability. Our students should therefore be abreast with socio-cultural changes and learn about sustainable development in the context of rapidly changing markets.

### ***Basic research in food safety, tolerance limits, nutrigenomics and functional foods***

The science and technology of Nutrition and health foods is advancing rapidly as at no other time. Health conscious consumers seek health foods. If the markets refuse to be science-driven, quacks and false claims will move in. For ensuring quality control and to test claims, labs will be needed. These labs should be able to conduct basic research at the molecular level. The understanding of health and disease, and its management through genomics are challenges for the future. The Nutrition professional should gear up to meet these challenges.

### **Education policy**

We have a long way to go, and a lot needs to be done in traditional institutions. The universities should begin to invest in laboratories for Nutrition education, and motivate their faculty to work scientifically. They should work with global collaboration where adequate facilities exist. These collaborations should be for research, staff capacity building, and study-abroad programmes. What is easily achievable by restructuring the syllabus is interdisciplinary education. Postgraduate students in Nutrition should take interdisciplinary examinations on economics, public health, food technology and control of plant diseases, and plant genetics. Similarly, students of these various disciplines should study Nutrition.

### **Opportunities**

India has a great requirement for qualified nutritionists. The formal training of nutrition personnel takes place through Agriculture universities and UGC-run universities. Given that Nutrition is interdisciplinary in nature, many scientists delve into certain specialized areas. The Home Science network is very widespread through all the States and even in remotely located educational institutions. The distinct advantage is that they understand local community needs. The limitations are that depth of training is variable due to variable local concerns and there is no planned government outlay for professionals.

Most of the institutions endeavour to achieve the following professional competencies:

- Entrepreneurship- in catering, health foods
- Mobilization of local NGO/Self help groups- infant feeding, immunization and supplementary feeding, MDM meal supply
- Programme planning and evaluation- ICDS, MDM, anaemia control
- Institutional food administration- hospitals, school meals, home catering
- Diet counselling- through life-cycle approach, dietetics, community nutrition education

The Ministry of WCD should set up field nutrition counselling units with qualified dietitians instead of anganwadi workers. The Ministry of Health and Family Welfare should insist on hospital dietitians in all private and government hospitals to monitor and advise on the nutritional adequacy of diets for patients.

I wish all our students a brilliant future and hope that our training will help them to work towards sustainable national development and empowerment. Remember this is achievable with strong team building.

# OMEGA-6/OMEGA-3 RATIO: THE GOLDEN BALANCE

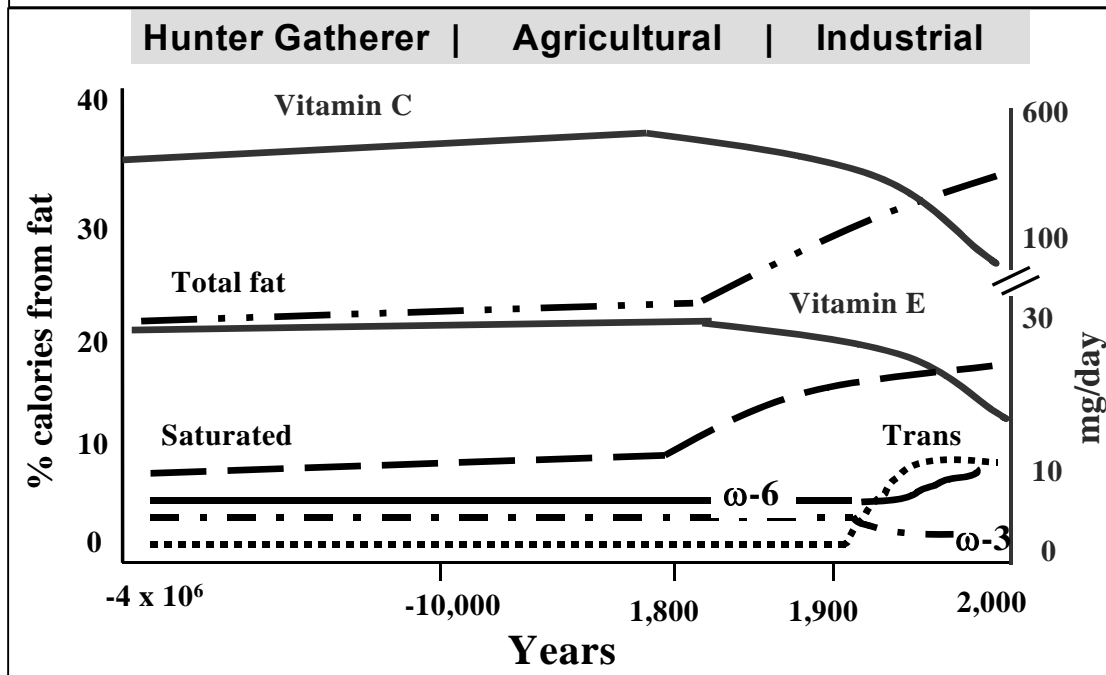
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## Introduction

Major changes have taken place in our diets over the past 10,000 years since the beginning of the Agricultural Revolution, but our genes have not changed<sup>1-6</sup>. The spontaneous mutation rate for nuclear DNA is estimated at 0.5% per million years. Therefore, over the past 10,000 years there has been time for very little change in our genes, perhaps 0.005%. In fact, our genes today are very similar to the genes of our ancestors during the Paleolithic period 40,000 years ago, at which time our genetic profile was established<sup>7</sup>. Humans today

Figure 1: Hypothetical scheme of fat, fatty acid ( $\omega$  6,  $\omega$  3, trans and total) intake (as percent of calories from fat) and intake of vitamins E and C (mg/d). Data were extrapolated from cross-sectional analyses of contemporary hunter-gatherer populations and from longitudinal observations and their putative changes during the preceding 100 years<sup>9</sup>



live in a nutritional environment that differs from that for which our genetic constitution was selected. Studies on the evolutionary aspects of diets indicate that major changes have taken place in our diets, particularly in the type and amount of essential fatty acids and in the antioxidant content of foods<sup>7-11</sup> (Figure 1).

Today's industrialized societies are characterized by:

- an increase in energy intake and decrease in energy expenditure;
- an increase in the intake of saturated fats, omega-6 fatty acids and trans fatty acids, and a decrease in the intake of omega-3 fatty acids;
- a decrease in the intake of complex carbohydrates and fiber;
- an increase in the intake of cereal grains and a decrease in the intake of fruits and vegetables; and

- a decrease in the intake of proteins, antioxidants and calcium<sup>7,9,12-16</sup> (Tables 1 and 2).

The increase in *trans* fatty acids is detrimental to health as shown in Table 3<sup>17</sup>. In addition, *trans* fatty acids interfere with the desaturation and elongation of both omega-6 and omega-3 fatty acids, thus further decreasing the amount of arachidonic acid, eicosapentaenoic acid and docosahexaenoic acid availability for human metabolism<sup>18</sup>

The beneficial health effects of omega-3 fatty acids, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) were described first in the Greenland Eskimos who consumed a diet rich in seafood and had low rates of coronary heart disease, asthma, Type 1 diabetes mellitus, and multiple sclerosis. Since that observation, the beneficial health effects of omega-3 fatty acids have been extended to include benefits related to cancer, inflammatory bowel disease, rheumatoid arthritis, and psoriasis<sup>19</sup>.

Whereas evolutionary maladaptation leads to reproductive restriction (or differential fertility), the rapid changes in our diets, particularly over the past 150 years, are potent promoters of chronic diseases such as atherosclerosis, essential hypertension, obesity, diabetes, arthritis and other autoimmune diseases, and many cancers, especially cancer of the breast<sup>20</sup>, colon<sup>21</sup>, and prostate<sup>22</sup>. In addition to diet, sedentary lifestyles and exposure to noxious substances interact with genetically controlled biochemical processes, leading to chronic diseases.

In this review, I discuss the importance of the balance of omega-6 and omega-3 essential fatty acids in the prevention and treatment of coronary artery disease, hypertension, diabetes, arthritis, osteoporosis, other inflammatory and autoimmune disorders, cancer, and mental health, and the mechanisms involved. I selected this topic because it is relevant to the Indian population, particularly those who are vegetarian, since their diet is characterized by high linolenic acid/alpha-linolenic acid ratio, given that diets have recently seen an increase in vegetable oils such as corn and sunflower oils that are very high in linolenic acid (66% and 77%, respectively).

### Imbalance of Omega-6/Omega-3

Food technology and agribusiness provided the economic stimulus that dominated the changes in the food supply<sup>23, 24</sup>. From per capita quantities of foods available for consumption in the U.S. national food supply in 1985, the

**Table 1: Estimated omega-3 and omega-6 fatty acid intake in the late Paleolithic period (g/d)<sup>a,b</sup>**

Plants	
LA	4.28
ALA	11.40
Animals	
LA	4.56
ALA	1.21
Total	
LA	8.84
ALA	12.60
Animal	
AA (ω 6)	1.81
EPA.( ω 3)	0.39
DTA (ω 6)	0.12
DPA (ω 3)	0.42
DHA.( ω 3)	0.27
Ratios of ω 6/ ω 3	
LA/ALA	0.70
AA+DTA/EPA+DPA+DHA	1.79
Total ω 6/ ω 3	0.79 <sup>b</sup>
LA, linoleic acid; ALA, linolenic acid; AA, arachidonic acid; EPA, eicosapentaenoic acid; DTA, docosatetraenoic acid; DPA, docosapentaenoic acid; DHA, docosahexaenoic acid.	
<sup>a</sup> Data from Eaton et al. <sup>13</sup> .	
<sup>b</sup> Assuming an energy intake of 35:65 of animal: plant sources.	

amount of EPA is reported to be about 50 mg per capita/day and the amount of DHA is 80 mg per capita/day. The two main sources are fish and

	Late Paleolithic <sup>1</sup>	FNB-IOM 1989 Recommendations <sup>1</sup>	FNB-IOM 2005 Recommendations <sup>2</sup>
Total dietary energy, (%)			
Protein	33	12	10-35
Carbohydrate	46	58	45-65
Fat	21	30	20-35
Alcohol	~0	0	0
P/S ratio	1.41	1.00	0
Cholesterol (mg)	520	300	<300
Fiber (g)	100-150	30-60	38
Sodium (mg)	690	1100-3300	<2300
Sodium (mg)	690	1100-3300	<2300
Ascorbic acid (mg)	440	60	75

<sup>1</sup>Modified from Eaton et al.<sup>13</sup>.  
P/S = polyunsaturated to saturated fat  
<sup>2</sup>Data from DRI Tables on the internet:  
<http://www.iom.edu/CMS/3788/4574.aspx>

poultry<sup>25</sup>. It has been estimated that the present Western diet is “deficient” in omega-3 fatty acids with a ratio of omega-6 to omega-3 of 15-20/1, instead of 1/1 as is the case in the diets of wild animals, and presumably should be in the diets of human beings<sup>7-11, 13,26-28</sup> (Table 4).

<b>Decrease or inhibit</b>
Decrease or inhibit incorporation of other fatty acids into cell membranes
Decrease high-density lipoprotein (HDL)
Inhibit delta-6 desaturase (interfere with elongation and desaturation of essential fatty acids)
Decrease serum testosterone (in male rats)
Cross the placenta and decrease birth weight (in humans)
<b>Increase</b>
Low-density lipoprotein (LDL)
Platelet aggregation
Lipoprotein (a) [Lp(a)]
Body weight
Cholesterol transfer protein (CTP)
Abnormal morphology of sperm (in male rats)
Modified from reference <sup>17</sup>

Before the 1940s cod-liver oil was ingested mainly by children as a source of vitamin A and vitamin D with the usual dose being a teaspoon. Once these vitamins were synthesized, consumption of cod-liver oil was drastically decreased, contributing further to the decrease in EPA and DHA intake. Table 5 shows ethnic

differences in fatty acid concentrations in thrombocyte phospholipids, the ratios of omega-6/omega-3 fatty acids, and percentage of all deaths from cardiovascular disease<sup>16</sup>. An absolute and relative change of omega-6/omega-3 has occurred in the food supply of Western societies over the past 150 years. A balance existed between omega-6 and omega-3 for millions of years during the long evolutionary history of the genus Homo, and genetic changes occurred partly in

	Paleolithic	Western
LA:ALA	0.70	18.75
AA+DTA:EPA+DPA+DHA	1.79	3.33
Total	0.79	16.74

LA, linoleic acid; ALA, linolenic acid; AA, arachidonic acid; EPA, eicosapentaenoic acid; DTA, docosatetraenoic acid; DPA, docosapentaenoic acid; DHA, docosahexaenoic acid. Reprinted with permission from reference<sup>15</sup>.

response to these dietary influences.

During evolution, omega-3 fatty acids were found in all foods consumed: meat, wild plants, eggs, fish, nuts and berries<sup>29-38</sup>. Studies by Cordain *et al.*<sup>39</sup> on wild animals confirm the original observations of Crawford and Sinclair *et al.*<sup>27,40</sup>. However, rapid dietary changes over short

periods of time, as have occurred over the past 100-150 years, are a totally new phenomenon in human evolution<sup>13, 15,41-43</sup> (Table 6).

**Table 5: Ethnic differences in fatty acid concentrations in thrombocyte phospholipids and percentage of all deaths from cardiovascular disease<sup>1</sup>**

	Europe and United States	Japan	Greenland Eskimos
Arachidonic acid (20:4 ω 6)	26	21	8.3
Eicosapentaenoic acid (20:5 ω 3)	0.5	1.6	8.0
Ratio of ω 6 to ω 3	50	12	1
CVD as % of all deaths	45	12	7

<sup>1</sup>Data modified from reference<sup>16</sup>.

**Table 6: Omega-6:Omega-3 Ratios in Various Populations**

Population	ω 6/ ω 3	Reference
Paleolithic	0.79	13
Greece prior to 1960	1.00 – 2.00	15
Current Japan	4.00	41
Current India, rural	5 – 6.1	42
Current United Kingdom and northern Europe	15.00	43
Current United States	16.74	13
Current India, urban	38 – 50	42

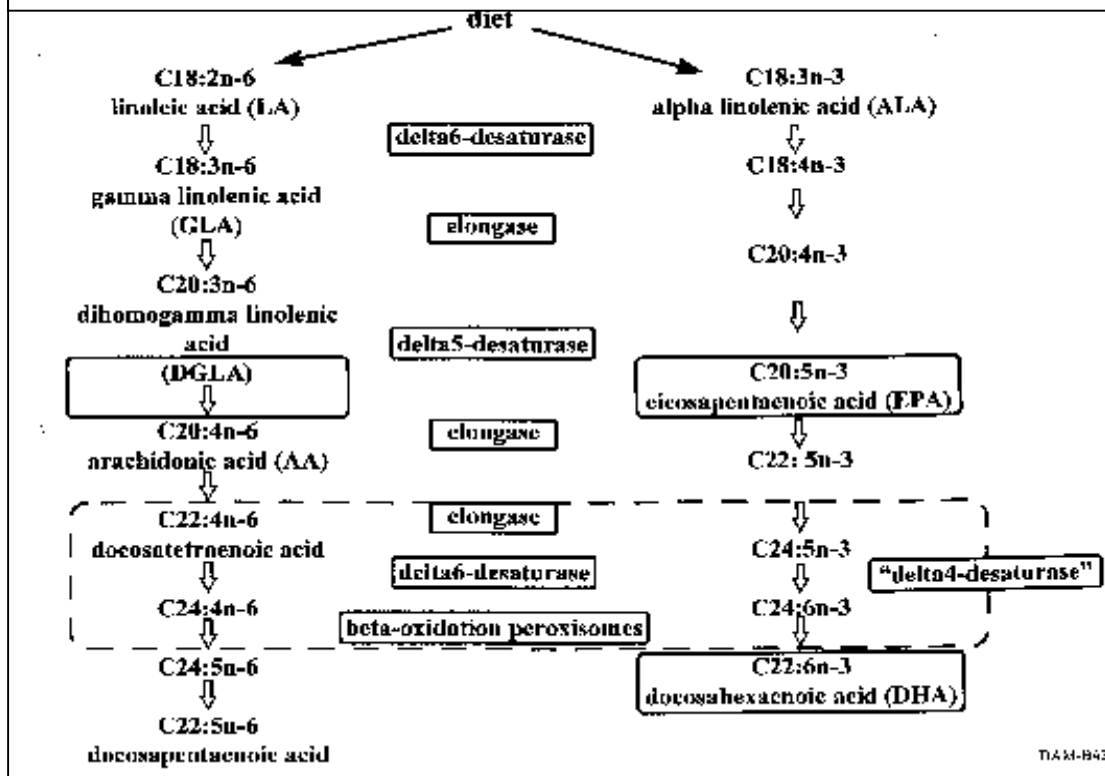
### Biological Effects and the Omega-6/Omega-3 Ratio

There are two classes of essential fatty acids (EFA), omega-6 and omega-3. The distinction between omega-6 and omega-3 fatty acids is based on the location of the first double bond, counting

from the methyl end of the fatty acid molecule. In the omega-6 fatty acids, the first double bond is between the 6<sup>th</sup> and 7<sup>th</sup> carbon atoms, and in the omega-3 fatty acids the first double bond is between the 3<sup>rd</sup> and 4<sup>th</sup> carbon atoms. Monounsaturates are represented by oleic acid, an omega-9 fatty acid, which can be synthesized by all mammals including humans. Its double bond is between the 9<sup>th</sup> and 10<sup>th</sup> carbon atoms.

Omega-6 and omega-3 fatty acids are essential because humans, like all mammals, cannot make them and must obtain them from their diets. Omega-6 fatty acids are represented by linoleic acid (LA; 18:2 ω 6) and omega-3 fatty acids by α-linolenic acid (ALA; 18:3 ω 3). LA is plentiful in nature and is found in the seeds of most plants except coconut, cocoa, and palm. ALA on the other hand is found in the chloroplasts of green leafy vegetables, and in the seeds of flax, rape, and perilla, and in walnuts. Both EFAs are metabolized to longer-chain fatty acids of 20 and 22 carbon atoms. LA is metabolized to arachidonic acid (AA; 20:4ω6), and LNA to EPA (20:5 ω 3) and DHA (22:6 ω 3), increasing the chain length and degree of unsaturation by adding extra double bonds to the carboxyl end of the fatty acid molecule (Figure 2).

Figure 2: Elongation and desaturation of omega-6 and omega-3 polyunsaturated fatty acids



Humans and other mammals, except for carnivores such as lions, can convert LA to AA and ALA to EPA and DHA, but the conversion is slow<sup>44</sup>. This conversion was shown by using deuterated ALA<sup>45</sup>. There is competition between omega-6 and omega-3 fatty acids for the desaturation enzymes. However, both  $\alpha$ -4 and  $\alpha$ -6 desaturases prefer omega-3 to omega-6 fatty acids<sup>44, 46,47</sup>. But a high LA intake interferes with the desaturation and elongation of ALA<sup>45,48</sup>. Trans fatty acids interfere with the desaturation and elongation of both LA and ALA.  $\alpha$ -6 desaturase is the limiting enzyme, and there is some evidence that it decreases with age<sup>44</sup>. Premature infants<sup>49</sup>, hypertensive individuals<sup>50</sup>, and some diabetics<sup>51</sup> are limited in their ability to make EPA and DHA from ALA. These findings are important and need to be considered when making dietary recommendations. EPA and DHA are found in the oils of fish, particularly fatty fish. AA is found predominantly in the phospholipids of grain-fed animals and in eggs.

Table 7: Effects of Ingestion of EPA and DHA from Fish or Fish Oil	
➤	A decrease in the production of prostaglandin E <sub>2</sub> (PGE <sub>2</sub> ) metabolites
➤	A decrease in thromboxane A <sub>2</sub> , a potent platelet aggregator and vasoconstrictor
➤	A decrease in the formation of leukotriene B <sub>4</sub> , an inducer of inflammation, and a powerful inducer of leukocyte chemotaxis and adherence
➤	An increase in thromboxane A <sub>3</sub> , a weak platelet aggregator and weak vasoconstrictor
➤	An increase in prostacyclin PGI <sub>3</sub> , leading to an overall increase in total prostacyclin by increasing PGI <sub>3</sub> without a decrease in PGI <sub>2</sub> , both PGI <sub>2</sub> and PGI <sub>3</sub> are active vasodilators and inhibitors of platelet aggregation
➤	An increase in leukotriene B <sub>5</sub> , a weak inducer of inflammation and a weak chemotactic agent

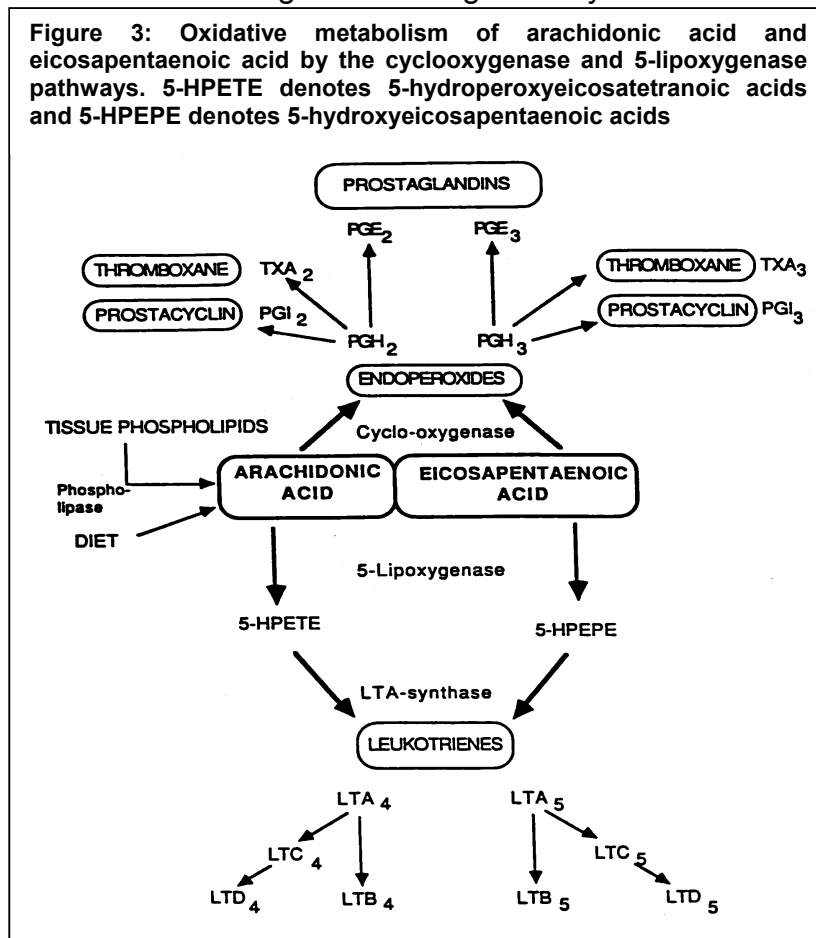
LA, ALA, and their long-chain derivatives are important components of animal and plant cell membranes. In mammals and birds, the omega-3 fatty acids

are distributed selectively among lipid classes. ALA is found in triglycerides, in cholesteryl esters, and in very small amounts in phospholipids. EPA is found in cholesteryl esters, triglycerides, and phospholipids. DHA is found mostly in phospholipids. In mammals, including humans, the cerebral cortex, retina, testis, and sperm are particularly rich in DHA. DHA is one of the most abundant components of the brain's structural lipids. DHA, like EPA, can be derived only from direct ingestion or by synthesis from dietary EPA or ALA.

Mammalian cells cannot convert omega-6 to omega-3 fatty acids because they lack the converting enzyme, omega-3 desaturase.

LA, the parent omega-6 fatty acid, and ALA, the parent omega-3 fatty acid, and their long-chain derivatives are important components of animal and plant cell membranes (Figure 2). These two classes of EFA are not interconvertible, are metabolically and functionally distinct, and often have important opposing physiological

**Figure 3: Oxidative metabolism of arachidonic acid and eicosapentaenoic acid by the cyclooxygenase and 5-lipoxygenase pathways. 5-HPETE denotes 5-hydroperoxyeicosatetraenoic acids and 5-HPEPE denotes 5-hydroxyeicosapentaenoic acids**



functions. When humans ingest fish or fish oil, the EPA and DHA from the diet partially replace the omega-6 fatty acids, especially AA, probably in the membranes of all cells, but especially in the membranes of platelets, erythrocytes, neutrophils, monocytes, and liver cells (reviewed in references<sup>52</sup>). Whereas cellular proteins are genetically determined, the polyunsaturated fatty acid (PUFA) composition of cell membranes is to a great extent dependent on the dietary intake. AA and EPA are the parent compounds for eicosanoid production<sup>8</sup> (Tables 7-8, Figure 3).

Because of the increased amounts of omega-6 fatty acids in the Western diet, the eicosanoid metabolic products from AA, specifically prostaglandins, thromboxanes, leukotrienes, hydroxy fatty acids, and lipoxins, are formed in larger quantities than those formed from omega-3 fatty acids, specifically EPA<sup>8</sup>. The eicosanoids from AA are biologically active in very small quantities and, if they are formed in large amounts, they contribute to the formation of



thrombus and atheromas; to allergic and inflammatory disorders, particularly in susceptible people; and to proliferation of cells. Thus, a diet rich in omega-6 fatty acids shifts the physiological state to one that is prothrombotic and proaggregatory, increases blood viscosity, vasospasm and vasoconstriction and decreases in bleeding time. Bleeding time is decreased in groups of patients with hypercholesterolemia, hyperlipoproteinemia, myocardial infarction, other forms of atherosclerotic disease, and diabetes (obesity and hypertriglyceridemia). Bleeding time is longer in women than in men and longer in young people than in older ones. There are ethnic differences in bleeding time that appear to be related to diet.

## **Mechanisms**

### ***Linoleic acid increases low-density lipoprotein oxidation and severity of coronary atherosclerosis***

Oxidative modification increases the atherogenicity of low-density lipoprotein (LDL) cholesterol. Oxidized LDL is taken up by scavenger receptors that do not recognize unmodified LDL, leading to foam cell formation. Diets enriched with LA increase the LA content of LDL and its susceptibility to oxidation<sup>53, 54</sup>. Reaven *et al.*<sup>55</sup> showed that a LA-enriched diet especially affects oxidation of small, dense LDL. Louheranta *et al.*<sup>56</sup> showed that as the percent of energy intake from LA increased from the lower quartile 2.9% to the highest 6.4% so did the LDL oxidation. In their study, the average energy from LA was 4.6%. In another small cross-sectional study, the enhanced susceptibility of LDL to oxidation was associated with severity of coronary atherosclerosis<sup>57</sup>.

### ***Linoleic acid inhibits eicosapentaenoic acid Incorporation from dietary fish oil supplements in human subjects***

Cleland *et al.* showed that LA inhibits EPA incorporation from dietary fish oil supplements in human subjects<sup>58</sup>. Thirty healthy male subjects were randomly allocated into one of two treatment groups. One group was on a high LA and low saturated fatty acid diet, whereas the other group was on a low LA and low saturated fat diet. The shortfall in the low LA and low saturated fatty acid diet was made up with monounsaturated fatty acids (olive oil). After a 3-week run-in period, the subjects consumed a fish oil supplement containing 1.6 g EPA and 0.32 g DHA per day. After four weeks of fish oil supplementation, the incorporation of EPA in neutrophil membrane phospholipids was highest in the lowest LA group, indicating that the ingestion of omega-6 fatty acids in the diet is an important determinant of EPA incorporation into neutrophil membranes. This study also shows that monounsaturated fatty in this case olive oil; do not interfere with EPA incorporation

### ***Decreasing linoleic acid with constant $\alpha$ -linolenic acid in dietary Fats inceases (omega-3) eicosapentaenoic acid in plasma phospholipids in healthy men***

Liou *et al.* carried out a study in which decreasing levels of LA with constant ALA led to increases of EPA in plasma phospholipids in healthy men<sup>59</sup>. The

omega-6/omega-3 dietary ratio varied between 10/1 and 4/0 of LA/ALA. It is unfortunate that the authors did not have a lower ratio of 2-1/1 omega-6/omega-3, which is closer to the ratio in diets on which humans evolved. At a ratio of 1/1, Zampelas *et al.* showed a decrease in C-reactive protein (CRP), which Liou *et al.*, at a ratio of 4/1, did not show<sup>60</sup>.

Factor	Function	Effect of n-3 fatty acid
Arachidonic acid	Eicosanoid precursor; aggregates platelets; stimulates white blood cells	↓
Thromboxane A <sub>2</sub>	Platelet aggregation; vasoconstriction; increase of intracellular Ca <sup>++</sup>	↓
Prostacyclin (PGI <sub>2/3</sub> )	Prevent platelet aggregation; vasodilation; increase cAMP	↑
Leukotriene (LTB <sub>4</sub> )	Neutrophil chemoattractant; increase of intracellular Ca <sup>++</sup>	↓
Fibrinogen	A member of the acute phase response; and a blood clotting factor	↓
Tissue plasminogen activator	Increase endogenous fibrinolysis	↑
Platelet activating factor (PAF)	Activates platelets and white blood cells	↓
Platelet-derived growth factor (PDGF)	Chemoattractant and mitogen for smooth muscles and macrophages	↓
Oxygen free radicals	Cellular damage; enhance LDL uptake via scavenger pathway; stimulate arachidonic acid metabolism	↓
Lipid hydroperoxides	Stimulate eicosanoid formation	↓
Interleukin 1 and tumor necrosis factor	Stimulate neutrophil O <sub>2</sub> free radical formation; stimulate lymphocyte proliferation; stimulate PAF; express intercellular adhesion molecule-1 on endothelial cells; inhibit plasminogen activator, thus, procoagulants	↓
Interleukin-6	Stimulates the synthesis of all acute phase proteins involved in the inflammatory response: C-reactive protein; serum amyloid A; fibrinogen; α <sub>1</sub> -chymotrypsin; and haptoglobin	↓
C-reactive protein (CRP)	An acute phase reactant and an independent risk factor for cardiovascular disease	↓
Endothelial-derived relaxation factor	Reduces arterial vasoconstrictor response	↑
Insulin function		Increases sensitivity to insulin
VLDL	Related to LDL and HDL level	↓
HDL	Decreases the risk for coronary heart disease	↑
Lp(a)	Lipoprotein(a) is a genetically determined protein that has atherogenic and thrombogenic properties	↓
Triglycerides and chylomicrons	Contribute to postprandial lipemia	↓

### ***A lower omega-6/omega-3 ratio as part of a Mediterranean diet decreases vascular endothelial growth factor***

Ambring *et al.* studied the ratio of serum phospholipid omega-6 to omega-3 fatty acids, the number of leukocytes and platelets, and vascular endothelial growth factor (VEGF) in healthy subjects on an ordinary Swedish diet and on a Mediterranean-inspired diet that was high in fish and flaxseed oil<sup>61</sup>. This is a very interesting and important study, because it clearly showed that the serum phospholipid ratio of omega-6/omega-3 fatty acids was substantially lowered with the Mediterranean diet as compared to the Swedish diet. The omega-6/omega-3 ratio was  $4.72 \pm 0.19$  with the Swedish diet and  $2.60 \pm 0.19$  with the Mediterranean diet ( $p < 0.0001$ ). There was no change in CRP or interleukin-6 (IL-6), but the total number of leukocytes was 10% lower after the Mediterranean diet, the total number of platelets was 15% lower, and so was the serum VEGF,  $206 \pm 25$  pg/mL as against  $237 \pm 30$  after the Swedish diet ( $p = 0.0014$ ). The authors concluded, "A Mediterranean-inspired diet reduces the number of platelets and leukocytes and VEGF concentrations in healthy subjects. This may be linked to higher serum concentrations of omega-3 fatty acids, which promote a favorable composition of phospholipids." These findings are consistent with our studies on the traditional diet of Greece prior to 1960 that was rich in ALA, EPA and DHA and balanced in the omega-6/omega-3 ratio, which distinguished it from other Mediterranean diets<sup>62,63</sup>, by being similar in the omega-6/omega-3 ratio to the diet on which human beings evolved<sup>7-13,26-28</sup>.

### ***A reduced omega-6/omega-3 fatty acid dietary ratio increases adiponectin concentration and fatty acid oxidation in healthy subjects***

Guebre-Egziabher *et al.* carried out a ten-week dietary intervention in 17 healthy subjects<sup>64</sup>. The dietary intervention decreased the LA/ALA ratio from  $32.2 \pm 3.7$  to  $2.2 \pm 0.1$ . Dietary intake, euglycemic hyperinsulinemic clamp, indirect calorimetry, lipid profile, hormones, inflammatory markers and erythrocyte membrane fatty acid composition were measured before and at the end of the intervention period. Comparisons are between baseline and post-intervention levels. There were significant decreases in glucose oxidation rate, in LDL, and TNF- $\alpha$ , with a non-significant decrease in IL-6 and CRP. Most importantly, there was a significant increase in adiponectin and fatty acid oxidation, which may explain the decrease in adipose tissue noted by Couet *et al.*<sup>65</sup>, and the weight loss noted by Hill *et al.*<sup>66</sup> as being associated with increased intakes of dietary omega-3 fatty acids. The Guebre-Egziabher *et al.* study showed that a decreased omega-6/omega-3 fatty acid ratio can be achieved with simple dietary counselling, resulting in multiple potentially favourable effects on the metabolic and inflammatory profiles of the subjects<sup>64</sup>.

### ***As the omega-6/omega-3 ratio decreases, so does the platelet aggregation***

Freese *et al.* compared the effects of two diets, rich in monounsaturated fatty acids and differing in their LA/ALA ratios, on platelet aggregation in human

volunteers<sup>67</sup>. The two diets were similar in saturated, monounsaturated and polyunsaturated fatty acids. The results showed that platelet aggregation *in vitro* decreases as the ratio of LA/ALA decreases in diets rich in monounsaturated fatty acids. The higher the ratio of omega-6/omega-3 fatty acids in platelet phospholipids, the higher is the death rate from cardiovascular disease<sup>16</sup>. Excessive amounts of omega-6 PUFA and a very high omega-6/omega-3 ratio, as is found in today's Western diets, promote the pathogenesis of many diseases, including cardiovascular disease, cancer, and inflammatory and autoimmune diseases, whereas increased levels of omega-3 PUFA (a lower omega-6/omega-3 ratio), exert suppressive effects<sup>68</sup>.

### ***Plasma omega-6 omega-3 ratio and inflammatory markers***

Ferrucci *et al.* studied the relationship of plasma PUFA to circulating inflammatory markers in 1123 persons aged 20 – 98 years in a community-based sample<sup>69</sup>. The total omega-3 fatty acids were independently associated with lower levels of pro-inflammatory markers IL-6, IL-1ra, tumor necrosis factor- $\alpha$  (TNF  $\alpha$ ), CRP), and higher levels of anti-inflammatory markers [soluble IL-6r, IL-10, transforming growth factor-  $\alpha$  (TGF  $\alpha$ ) independent of confounders. The omega-6/omega-3 ratio was a strong negative correlate of IL-10. The authors concluded, "Omega-3 fatty acids are beneficial in patients affected by diseases characterized by active inflammation."

### **The balance of omega-6/omega-3 fatty acids is important for health: evidence from gene transfer studies**

Further support for the need to balance the omega-6/omega-3 EFA comes from the studies of Kang *et al.*<sup>70, 71</sup>, which clearly show the ability of both normal rat cardiomyocytes and human breast cancer cells in culture to form all the omega-3's from omega-6 fatty acids when fed the cDNA encoding omega-3 fatty acid desaturase obtained from the roundworm *Caenorhabditis elegans* (*C. elegans*). The omega-3 desaturase efficiently and quickly converted the omega-6 fatty acids that were fed to the cardiomyocytes in culture to the corresponding omega-3 fatty acids. Thus, omega-6 LA was converted to omega-3 ALA and AA was converted to EPA, so that, at equilibrium, the ratio of omega-6 to omega-3 PUFA was close to 1/1. Further studies demonstrated that the cancer cells expressing the omega-3 desaturase underwent apoptotic death whereas the control cancer cells with a high omega-6/omega-3 ratio continued to proliferate<sup>72</sup>. More recently, Kang, *et al.* showed that transgenic mice and pigs expressing the *C. elegans fat-1* gene encoding an omega-3 fatty acid desaturase are capable of producing omega-3 from omega-6 fatty acids, leading to enrichment of omega-3 fatty acids with reduced levels of omega-6 fatty acids in almost all organs and tissues, including muscles and milk, with no need of dietary omega-3 fatty acid supply<sup>73-75</sup>. This discovery provides a unique tool and new opportunities for omega-3 research, and raises the potential for producing *fat-1* transgenic livestock as a new and ideal source of omega-3 fatty acids to meet human nutritional needs. Furthermore, the transgenic mouse model is being used widely by scientists for the study of chronic diseases and mechanisms underlying the beneficial effects of omega-3 fatty acids<sup>76</sup>.

## **Omega-3 fatty acids and gene expression**

Previous studies have shown that fatty acids released from membrane phospholipids by cellular phospholipases, or made available to the cell from the diet or other aspects of the extracellular environment, are important cell-signalling molecules. They can act as second messengers or substitute for the classical second messengers of the inositide phospholipid and the cyclic AMP signal transduction pathways. They can also act as modulator molecules mediating responses of the cell to extracellular signals. Recently it has been shown that fatty acids rapidly and directly alter the transcription of specific genes<sup>77</sup>. In the case of genes involved in inflammation, such as IL-1 $\alpha$ , EPA and DHA suppress IL-1 $\alpha$  mRNA whereas AA does not, and the same effect appears in studies on growth-related early response gene expression and growth factor<sup>77</sup>. In the case of vascular cell adhesion molecule (VCAM), AA has a modest suppressing effect relative to DHA. The latter situation may explain the protective effect of fish oil toward colonic carcinogenesis, since EPA and DHA did not stimulate protein kinase C. PUFA regulation of gene expression extends beyond the liver and includes genes such as adipocyte glucose transporter-4, lymphocyte stearyl-CoA desaturase 2 in the brain, peripheral monocytes (IL-1  $\alpha$ , and VCAM-1) and platelets [platelet derived growth factor (PDGF)]. Whereas some of the transcriptional effects of PUFA appear to be mediated by eicosanoids, the PUFA suppression of lipogenic and glycolytic genes is independent of eicosanoid synthesis, and appears to involve a nuclear mechanism directly modified by PUFA.

## **Linoleic acid and arachidonic acid increase atherogenesis: evidence from diet gene Interactions: genetic variation and omega-6 and omega-3 fatty acid intake in the risk for cardiovascular disease**

As discussed above, leukotrienes are inflammatory mediators generated from AA by the enzyme 5-lipoxygenase. Since atherosclerosis involves arterial inflammation, Dwyer *et al.* hypothesized that a polymorphism in the 5-lipoxygenase-gene promoter could relate to atherosclerosis in humans, and that this effect could interact with the competing 5-lipoxygenase substrates in the dietary intake<sup>78</sup>. The study consisted of 470 healthy middle-aged women and men from the Los Angeles Atherosclerosis study, randomly sampled. The investigators determined 5-lipoxygenase (5-LO) genotypes, carotid-artery intima thickness, markers of inflammation, CRP, IL-6, and dietary AA, EPA, DHA, LA, and ALA with the use of six 24-hour recalls of food intake. The results showed that 5-LO variant genotypes were found in 6.0 percent of the cohort. Mean intima-media thickness adjusted for age, sex, height and racial or ethnic group was increased by  $80 \pm 19 \mu\text{m}$  from among the carriers of two variant alleles as compared with the carrier of the common (wild-type) allele. In multivariate analysis, the increase in intima-media thickness among carriers of two variant alleles ( $62 \mu\text{m}$ ,  $p < 0.001$ ) was similar in this cohort to that associated with diabetes ( $64 \mu\text{m}$ ,  $p < 0.01$ ) the strongest common risk factor for cardiovascular disease. Increased dietary AA significantly enhanced the apparent atherogenic effect of the genotype, whereas increased dietary intake of omega-3 fatty acids EPA and DHA blunted this effect. Furthermore, the plasma level of CRP of two variant alleles was increased by a factor of 2, as

compared to that among carriers of the common allele. Thus, genetic variation of 5-LO identifies a subpopulation at increased risk for atherosclerosis. The diet-gene interaction further suggests that dietary omega-6 fatty acids promote, whereas marine omega-3 fatty acids EPA and DHA inhibit the leukotriene-mediated inflammation that leads to atherosclerosis in this subpopulation.

The prevalence of variant genotypes did differ across racial and ethnic groups, with higher prevalence among Asians and Pacific Islanders (19.4%), blacks (24.0 percent) and other racial or ethnic groups (18.2 percent) than among Hispanic subjects (3.6 percent) and non-Hispanic whites (3.1 percent). Increased intima-mediated thickness was significantly associated with intake of both AA and LA among carriers of the two variant alleles, but not among carriers of the common alleles. In contrast, the intake of marine omega-3 fatty acids was significantly and inversely associated with intima-media thickness only among carriers of the two variant alleles. Diet gene interactions were specific to these fatty acids and were not observed in the dietary intake of monounsaturated and saturated fat, or other measured fatty acids. The study constitutes evidence that genetic variation in an inflammatory pathway in this case the leukotriene pathway can trigger atherogenesis in humans. These findings could lead to new dietary and targeted molecular approaches for the prevention and treatment of cardiovascular disease according to genotype, particularly in the populations of non-European descent<sup>6</sup>.

## **Conclusions and recommendations**

Western diets are characterized by high omega-6 and low omega-3 fatty acid intake, whereas during the Paleolithic period when human's genetic profile was established, there was a balance between omega-6 and omega-3 fatty acids. Therefore, humans today live in a nutritional environment that differs from that for which our genetic constitution was selected. The balance of omega-6/omega-3 fatty acids is an important determinant in decreasing the risk for coronary heart disease, both in primary and secondary prevention. Increased dietary intake of LA leads to oxidation of LDL and platelet aggregation, and interferes with the incorporation of EPA and DHA in cell membrane phospholipids. Both omega-6 and omega-3 fatty acids influence gene expression. EPA and DHA have the most potent anti-inflammatory effects. Inflammation is the root cause of many chronic diseases, including coronary heart disease, diabetes, arthritis, cancer, osteoporosis, mental ill health, dry eye disease and age-related macular degeneration. Dietary intake of omega-3 fatty acids may prevent the development of diseases, particularly in persons with genetic variations, for example those with genetic variants at the 5-LO who are particularly susceptible to developing coronary heart disease. Chronic diseases are multigenic and multifactorial. It is quite possible that the therapeutic dose of omega-3 fatty acids will depend on the degree or severity of disease resulting from the genetic predisposition. In carrying out clinical intervention trials, it is essential to increase the omega-3 and decrease the omega-6 fatty acid intake in order to have a balanced omega-6 and omega-3 intake in the background diet. Both the dietary intake and plasma

levels or red cell membrane phospholipids should be determined before and after the intervention study

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# **INFLUENCE OF WHO / UNICEF CODES ON INFANT FEEDING PRACTICES IN SOUTH ASIA: THE SRI LANKAN EXAMPLE**

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*This is an opportunity to pay my respects to Dr. C. Gopalan, the intellectual, the scientist, and the towering lighthouse of this region in the field of nutrition, and to acknowledge his contributions to humankind. He has been at the forefront in spreading knowledge of maternal and child nutrition to all, especially to mothers. His example and that of my guru Prof. C.C.de Silva have influenced generations of pediatricians to stress the teaching of nutrition to health professionals and improve the awareness of the nutritional needs of people at all levels throughout the complete span of human life. Sri Lanka felicitates him on his 90<sup>th</sup> birth anniversary, congratulating him for his leadership and wishing him many more years of health and happiness.*

## **Introduction**

If we begin at the beginning, we have to examine why WHO/UNICEF initiated the International Code of Marketing of Breast-Milk substitutes.<sup>1</sup> It was the health issue: inappropriate feeding practices lead to infant malnutrition, morbidity (chiefly diarrhoea), and mortality. Research scientists like Scrimshaw<sup>2</sup> and Chandra<sup>3</sup> showed the association between morbidity and bottle-feeding. Poor sanitation in ill-equipped kitchens in the developing world and non-availability of safe running water heightened the problem. Among poorer segments of the population, the use of diluted feeds was another factor responsible for infant undernutrition. In Asia, rapid urbanization was associated with a reduction in the traditional practice of breast-feeding. It came to be looked upon as 'old-fashioned.' The trend towards bottle-feeding, on the other hand, was considered 'modern'. In Asia, our own research<sup>4</sup> and studies conducted by others like Valyaselvi et al<sup>5</sup> in Thailand and Prema<sup>6</sup> in Hyderabad confirmed that breast-feeding was best for the infant's well being.

## **Infant food industry**

NGO's had played an important role in exposing the strategies adopted by the infant food industry targeting the general public, especially mothers, so as to popularize harmful practices such as bottle-feeding, use of various infant formulae and expensive complementary (weaning) foods. The infant food industry played down the value of mother's milk and natural nutritious complementary foods introduced at the appropriate time. Weaning foods were introduced very early in the infant's life, and even earlier in the West. Thus, scientific evidence regarding the value of breast-feeding formed the basis of the promotional steps taken up by WHO/UNICEF to protect and promote appropriate infant feeding practices through nutrition education. This nutrition education was undertaken through mass media and interpersonal communication by health professionals and community social workers.

## **WHO / UNICEF expert meetings**

In 1979 a joint WHO / UNICEF meeting was held in Geneva to discuss this code. Member states, International organizations, non-governmental institutions, experts and representatives of the infant food industry participated. At that large gathering, chaired by the persuasive and diplomatic Dr. Fred Sai who was supported by eminent scientists like Drs Moses Behar from WHO and David Burgess and many others, the Breast Feeding Code was accepted amidst much opposition from the infant food industry. Member states, except the US, voted for acceptance of the Code.

A separate meeting was chaired by me as Chairperson of Maternal and Young Child Nutrition / SCN / UN to define the appropriate timing of complementary feeding. In view of the observed faltering of growth in early infancy<sup>7</sup>, it was recommended that complementary feeds should be introduced by the fourth month of the infant's life<sup>8</sup>. Prof. Waterlow vehemently opposed this timing, proposing the third month. But it was finally possible to convince him to agree with us, through the support of members of my committee like Yngve Hofvander, Shiela Perera, Kusum Shah, Barbara Underwood, Demisse Hapte and M. Rowland. At the national level, it was possible, with the help of local activists, to convince mothers about the numerous advantages of breast-feeding and the need to avoid the early introduction of bottle-feeding. It took a lot of effort to convince mothers that giving water and prelacteal feeds (like coriander water and weak tea) reduced the 'sucking power' of the infant as well as its thirst, and also increased the infant's vulnerability to infection.

## **Efforts to improve breast-feeding**

Maternity ward practices to minimize post-partum pain and modern anesthetics for Caesarean section procedures enabled mothers undergoing operative delivery to initiate early breast-feeding. Mothers were encouraged to put the child to the breast as early as within one hour after a normal delivery. Mothers had to be convinced that the sucking and letdown reflexes would improve milk output. Lactogogues were given to mothers who had difficulty in initiating lactation<sup>9 10</sup>. Alongside, efforts were made locally to extend maternity leave so that breast-feeding could be sustained. In our inter-country research project steered by Tom Marchione, and Elizabeth Helsing<sup>11</sup> in Sri Lanka, we noted that the prevalence of breast-feeding dropped precipitously at six weeks when workingwomen went back to their jobs. With extended maternity leave up to four months granted by the Minister for Health, supported by the Prime Minister at that time, Sri Lankan mothers regained their zeal for exclusive breast-feeding.

WHO / UNICEF efforts to promote mother's milk were rewarded by improvement in the practice of breast-feeding globally. Mother-child bonding improved, and there was increased paternal and community acceptance of breast-feeding. The hopes for better child survival were strengthened. Needless to say, there were tremendous economic advantages<sup>12</sup> for parents and governments and reduction in the import of infant milk foods.

## The baby friendly hospital initiative

The Baby Friendly Hospital proposal, piloted with great enthusiasm by Dr. James Strong of UNICEF, did not succeed at national level. It was weakened by misguided maternity ward nurses and overanxious fathers, perhaps encouraged by the infant food industry. The Code prohibits the distribution of infant formula samples directly to mothers. The food industry then turned to the sale of artificial complementary (weaning) foods. Mothers were neither motivated nor enthusiastic about complementary foods when infant growth faltered. The advantage of introducing the different tastes and textures of home-based foods was ignored because of the tasty commercial preparations in the market. Mothers (and fathers) need to persevere with nutritious blended mixtures to prevent early undernutrition, which commences at about six months of age in Sri Lanka and most South Asian countries. Cultural practices, such as auspicious ceremonies for introducing complementary feeds, which had been abandoned, are being reintroduced and reinforced as appropriate. The growing literacy among mothers has helped in this instance. In 2002, following the findings from many international studies monitored by UNICEF and WHO, WHO have recommended exclusive breast-feeding for six months, followed by appropriate complementary feeding and continued breast-feeding.

	Country	Score
1 <sup>st</sup>	Sri Lanka	116/150
2 <sup>nd</sup>	Bangladesh	91.5/150
3 <sup>rd</sup>	Maldives	88.5/150
4 <sup>th</sup>	Pakistan	75.5/150
5 <sup>th</sup>	Nepal	71.5/150
6 <sup>th</sup>	India	68/150
7 <sup>th</sup>	Afghanistan and Bhutan	30/150

Bottle teats are to be avoided not only for hygienic reasons but in order to neutralize mothers' inclination to use these as 'pacifiers'. Longer prevalence of lactational amenorrhea<sup>13</sup> has contributed to postponement of the next pregnancy. This has contributed to improvement in the mothers' nutritional status and reduced the loss of iron that accompanies the early onset of menses. Spacing of births through acceptance of family planning methods is another factor that has contributed to improvement in maternal nutrition. Although demand feeding is encouraged by all health workers, it should be discouraged in later months. The baby's clock is the stomach and if the stomach is not full, there will be a demand for feeding. However demand feeding should not destroy the mother's sleep and peace!

## Breast-feeding prevalence

Morbidity patterns have changed in Sri Lanka since the establishment of the code. Certainly, the incidence of diarrhoea has reduced in the pattern of childhood disease. With the high literacy rate in Sri Lanka, health awareness ranks high. Breast-feeding prevalence has improved from 25% reported in our earlier WHO Inter-country collaborative studies steered by Manuel Carballo, to about 80% at present. A recent International Baby Food Action Network (IBFAN) study<sup>14</sup> has shown that Sri Lanka ranked as the best among South Asian countries.

The role of the father as an important part of the family unit needs to be strengthened with the concept of paternity leave, recognized better in the West than in South Asia, needs to be popularized. Efforts and activity must be intensified within professional groups who are interested in promoting these WHO / UNICEF policies relating to maternal nutrition. Derrick and Pat Jelliffe<sup>15</sup> were unflinching in their efforts in promoting the concept of the Mother-Child Dyad, and we would do well to emulate their example. Recent scientific studies have provided evidence of many valuable immunological factors in mother's milk. Fears of increased risk of malignancy associated with the use of plastic bottles and teats are some of the newer issues that have helped in furthering mothers' acceptance of the value of breast-feeding.

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## **DR C GOPALAN AND A NUTRITION SECURE INDIA**

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### **Introduction**

For over 60 years, Dr C Gopalan has been drawing attention to the basic nutritional malady in our country, namely chronic under-nutrition, mostly resulting from inadequate purchasing power. He has therefore been advocating a food based approach to overcoming endemic protein-energy under-nutrition. He has also been emphasizing the need to shift our public policies from just food security at the aggregate level, to nutritional security at the level of every individual child, woman and man. Sustainable nutrition security involves concurrent attention to physical, economic and social access to balanced diet, safe drinking water, primary health care and education. In a predominantly agricultural country like ours, Dr Gopalan's pathway of achieving nutrition security through homegrown food is the most affordable and achievable method of realizing the goal of food for all. Considering the global food crisis and steep escalation in food prices, this is also the most prudent way of managing our nutrition safety net programmes.

The Government of India has recently introduced several well-funded national programmes like the National Food Security Mission and Horticulture Mission (total outlay of about Rs. 25,000 Crore) and the Rashtriya Krishi Vikas Yojana (outlay of Rs 25,000 crores). If the nutritional dimension is integrated in these programmes, we can find location-specific agricultural remedies to most of our nutritional maladies without additional cost. A nutrition-secure India is the best tribute we can pay to the life and work of Dr C Gopalan. More than anybody else, he has worked with great clarity of thought and rigour of scientific experimentation and analysis, in finding practical solutions to our chronic and widespread nutritional problems. In this article, I would like to briefly summarize how we can convert Dr Gopalan's vision into practical accomplishment at the level of every child, woman and man.

### **Alarming dimensions of endemic hunger**

India is home to a huge population of malnourished persons, and several studies have established that high levels of malnutrition have a negative impact on human productivity and economic growth. According to UNESCO's Global Monitoring Report 2007, 47% of India's children are malnourished. Data from NHFS 3 shows that<sup>1</sup> 39 per cent of rural women in the 15-49 age group suffer from chronic energy deficiency and 58 per cent are anaemic. Among rural children between 6 – 35 months of age, 81 per cent are anaemic and 41 per cent are stunted, 49 per cent are under weight and 20 per cent suffer from wasting – all indicators of chronic and acute undernutrition. Stunted growth is a primary manifestation of malnutrition in early childhood including malnutrition during fetal development brought on by a malnourished mother, and the effects are irreversible. Low-birth-weight babies resulting from maternal and foetal undernutrition suffer from many handicaps including

reduced cognitive ability. Clearly, concerted efforts are needed to break the vicious circle (mother-child-mother) of malnutrition among the poor.

The high levels of malnutrition are pointers to the poor state of maternal and child health care services in the country. Sanitation, access to safe drinking water and health care can reduce the nutritional toll of infections. Ill health or endemic disease can perpetuate undernourishment. Morbidity reduces the ability of a person to ingest food. Some of the important non-food factors that can alleviate undernutrition are: access to health services, access to quick and effective medical attention, knowledge of nutrition, appropriateness of nutrition practices pertaining to dietary patterns, child care, sanitary arrangements, provision of safe drinking water as well as water for other needs, and eradication of infectious epidemics. The India Infrastructure Report 2007<sup>2</sup> highlights the lack of adequate infrastructure and personnel at public health care facilities as major problems on the rural health infrastructure front.

Water-related diseases are the single largest cause of sickness and death in the world, and they disproportionately affect poor people. Water-borne diseases are caused by viral or bacteriological contamination of water. The contamination can occur either due to unsanitary environmental conditions, improper storage and use at home, or both. Non-availability of safe drinking water and sanitary facilities may result in: increased exposure to infections resulting in diarrhoea and worm infestation; unnecessary loss of energy and time particularly if water and sanitary facilities are located far away from homes; and toxicity such as contamination of water with arsenic and fluoride due to over-exploitation of water resources. In India there are significant inter-State variations in terms of access to sanitation and water facilities. Access to toilet facilities is much less in rural areas and among the Scheduled Caste and Scheduled Tribe households<sup>3</sup>. The situation regarding access to safe drinking water is not heartening either. This, coupled with poor primary health care facilities and infrastructure, does not bode well for the food security in rural India.

### **Action plan for a nutrition-secure India**

The National Commission on Farmers (NCF)<sup>4</sup>, in its comprehensive report to the Government of India, has put forward a number of suggestions on methods to ensure food and nutrition security for all. It makes the point that, 'In a country with a high prevalence of poverty and malnutrition, the Government of India should always retain a commanding position in the management of the food security system'. It says further that, 'Food security with domestically grown foodgrains can alone eradicate widespread rural poverty and malnutrition, since farming is the backbone of the livelihood security system in rural India. This will enable Government to remain at the commanding height of the national food security system in a food crisis-ridden world. Building a food security system and containing the price rise with imported foodgrains may sometimes be a short-term necessity; but, in the long term, it will be a disaster to our farmers and farming.' The NCF makes the important point that, 'Building a sustainable food security system will



require attention to both the availability of sufficient food grain stocks and who controls them<sup>5</sup>.

The observations of the NCF are of great relevance in the context of the present food security situation in India; the situation has worsened over the past decade. All three aspects of food security availability of food, access to food, and absorption of food have been impacted negatively by incorrect policies such as inappropriate subsidy reduction and misplaced targeting. A strategy to ensure food and nutrition security for all has to pay concurrent attention to availability, access and absorption.

## **Hunger free India – components of action plan**

### ***Reform of the nutrition safety net delivery system***

The overall approach should be life cycle based and should involve appropriate supplementation programmes. The delivery systems relating to all nutrition support programmes should be restructured on a lifecycle basis, starting with pregnant women and infants 0-2 years of age, and ending with old and infirm persons. Elected Panchayats and local bodies should be involved in restructuring the delivery system.

The policy should promote the establishment of **Community Grain and Water Banks**, with the involvement of Panchayats and other local bodies. This programme should be based on the principle “store grain and water everywhere”.

### ***Eradication of hidden hunger***

Hidden hunger caused by micronutrient deficiencies must be addressed on the basis of natural food-cum-food fortification approaches. Food and nutrition security needs to be addressed through integrated complementary strategies, namely dietary diversification, supplementation, food fortification and community and public health measures.

### ***New deal for the self-employed***

The menu of income-earning opportunities for the self-employed needs to be enlarged. This calls for a paradigm shift from micro-finance to livelihood finance. Capacity Building and Mentoring Centres for self help groups (SHG) should be established.

### ***Enhancing the productivity and profitability of small holdings***

Agriculture is the backbone of the livelihood security system for two-thirds of India's population, and farmers constitute the largest proportion of consumers. The smaller the farm, the greater is the need for marketable surplus in order to get cash income. Hence, improvement of small-farm productivity, as a single development strategy, can make the greatest contribution to the

elimination of hunger and poverty. Fortunately, the untapped yield reservoir is high in most farming systems.

### ***Designing and introducing a food guarantee act***

A National Food Guarantee Act, combining the features of the Food for Work and Employment Guarantee Programmes, will represent a win-win situation both for producers and consumers. Following up on the National Rural Employment Guarantee Act (NREGA) and recognizing that the right to food and the right to livelihood are intimately related, we need to move towards a comprehensive “Food Guarantee Act”. Increased consumption will also stimulate greater production.

Building a sustainable food security system will require attention both to the availability of sufficient stocks and to those who control them. A Pan-political Party, National Food Security and Sovereignty Board with the Prime Minister as Chairperson can help to keep sustainable food security and sovereignty as a **National Common Minimum Programme** (in the same manner that UN Millennium Development Goals represent a global common minimum programme for Human Security).

### **Way ahead**

A National Consultation held at M S Swaminathan Research Foundation, Chennai, in 2006 arrived at the following recommendations. Recognizing that the majority of agricultural holdings in India are small, the focus must be on enhancing productivity, profitability and viability of smallholdings. For this purpose, we need to step up public investment in irrigation and rural infrastructure and provide other forms of State support including credit, post-harvest storage facilities such as rural warehouses, and processing. Such public investment may also address the issue of regional inequalities. With respect to irrigation, there should be a special focus on revitalization of existing local water storage systems and water bodies, and on decentralized community controlled systems of water use.

The Government must expand the minimum support price (MSP) system based on the cost of production, including a reasonable rate of return on investment and ensuring prompt and open-ended purchase of all major crops. Following up on the National Rural Employment Guarantee Act (NREGA), and recognising that the right to food and the right to livelihood are intimately related, we need to move towards a comprehensive “Food and Employment Guarantee Act”. Support of people’s movements must be enlisted to build popular consensus for such an Act. Also important is the support of the academic and scientific community.

While a universal PDS, appropriate supplementary feeding programmes and other safety nets funded by the government are critical for ensuring food security, there is also an important role for community-based food security systems, such as community grain banks<sup>8</sup>. Community food security systems appear especially relevant in socially cohesive communities characterised by

limited inequality, and in locations in which people find it difficult to access other delivery mechanisms such as PDS. Community food security systems may also be encouraged so that the production of nutritious millets, tuber crops and other local food grains receive much needed support. In order to ensure sustainability, such initiatives must work closely with elected local bodies. The overall approach of the delivery system should be life-cycle-based and involve appropriate supplementation programmes. The TPDS must be replaced by a universal PDS with uniform prices affordable by the poor. The centralisation that took place under the TPDS should be reversed, and State governments should, in the first instance, have the right to determine the required allocation under PDS for their State.

The allocation per household in the PDS should be based on the number of consumption units in the household. Besides rice or wheat, other relevant and nutritious food grains and pulses could be distributed through the PDS at subsidized rates, in order to enhance nutritional outcomes. Further, in order to improve the viability of Fair Price Shops, free-market commodities such as edible oil, cloth and other items of daily use could be sold through these outlets. Ration shops should be strengthened and made viable through the provision of adequate margins or subsidies. In order to ensure effective utilisation of the PDS, the public must be free to draw their allocations on a weekly basis. Migrants should be able to access the PDS wherever they happen to be working at the time.

Panchayati Raj Institutions (PRIs) should be actively involved in the monitoring of the PDS. PRIs should be empowered, trained and facilitated in monitoring hunger and malnutrition as well as schemes being implemented to reduce hunger/malnutrition such as Public Distribution System, Mid-day Meal Scheme, Integrated Child Development Services and Food for Work Programme. While food and nutrition insecurity need to be addressed at all stages of the life cycle, certain groups such as pregnant and lactating mothers, adolescents and children under three years of age need to be given special attention because of their physiological needs. Food and nutrition security should be addressed through integrated complementary strategies of dietary diversification, food supplementation, food fortification and community and public health measures

The economic policies should be reoriented to provide adequate support for India's agriculture and its vast rural population. In particular, policies must provide adequate rural infrastructure, including power, and promote employment, ensure credit and insurance facilities, and provide remunerative prices for produce. The unfinished agenda of land reforms must be completed and distribution of ceiling-surplus land must be done on a priority basis. Appropriate attention should be paid to the conservation of common community property and biodiversity resources, and the rehabilitation of wastelands. There should be a substantial increase in public investment in agriculture-related infrastructure such as irrigation and drainage, land development, water conservation and development of road connectivity. Such investments are especially needed in the poorer and low-rainfall areas of the country.

Substantial investments need to be made in health and education, especially for the rural population. These, along with reversal of macroeconomic policies to enhance aggregate demand, will improve the prospects of growth of rural employment. Quality employment has to be promoted. This requires enhancing the skill levels of the labour force on a large scale through massive training and capacity-building programmes, both by government and by the private sector. Village Knowledge Centres or Gyan Chaupals should be established in every Panchayat. A Nutrition-secure India is not an idle dream. It can be achieved sooner than most people may consider feasible, if we follow Dr Gopalan's pathway of ending hunger and malnutrition.

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# FRUITS AND VEGETABLES IN THE QUEST TO CONQUER DISEASE

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*Dr. C. Gopalan is a leading Indian authority on global nutrition and health. He has been active in the nutrition scene for more than sixty years. He upholds the concept of “holistic health” as opposed to merely combating nutrient deficiencies. Education and skill building are important for attaining his goal of a healthy society. Dr. Gopalan supports the improvement of the school system to include comprehensive health services. He believes that focused nutrition education targeted at adolescent girls, the mothers of tomorrow, will improve childrearing practices and household diets. Further, health and nutrition education should be part of the urban work places so as to encourage healthy lifestyles. Health is a basic right for all.*

*I am a nutritional biochemist working predominantly on assessment of vitamin A status and food-based approaches to ensure adequate vitamin A nutrition. My current age is less than the total time that Dr. Gopalan has been practicing nutrition and health awareness. Nonetheless, during my work as a nutrition scientist, I have learned to appreciate the importance of food-based approaches in ensuring adequate nutrition and general well-being. I not only believe that vegetables can make a difference in vitamin A nutrition, but also that when vegetables are eaten in sufficient quantities, they can help in the prevention and management of obesity and chronic diseases. Thus, I carry a torch similar to the one that Dr. Gopalan does, even though geographically he is in the southeast and I am in the northwest.*

## **Introduction**

In India, stunting and undernutrition are still prevalent in children from the poorer segments of the population. Furthermore, the rising prevalence of obesity and Type II diabetes mellitus among more affluent sections of the population are major health-related issues. As individuals move along the income continuum, oftentimes more money is available for purchasing food. Unfortunately, this money is usually spent on staple and snack foods that are inexpensive and readily available. Staple foods are typically high-starch and calorically dense, but not necessarily nutrient-dense. Snack foods tend to be high in fat and low in nutritional value. Therefore it is not surprising that, in India, the double burden of malnutrition exists. That is, undernutrition among the poor and overnutrition among those that have higher incomes. National and international food programmes have focused on providing communities with staple crops to meet the energy needs of people so that they may lead productive lives. These practices and policies endure, even though obesity rates continue to rise throughout the world. Food programmes need to be re-evaluated in order to promote healthful, nutritionally-dense diets such as those that include vegetables, rather than persisting with harmful energy-dense diets<sup>1</sup>.

## **Micronutrient deficiencies and food sources**

Globally, the most common micronutrient deficiencies are those of vitamin A, iron, and zinc. The ramifications of these deficiencies are known well to nutritionists. Children with vitamin A deficiency suffer from a decreased ability to fight infection, and often die if not treated. Severe vitamin A deficiency is one of the leading causes of childhood blindness. Iron deficiency results in anaemia. This negatively impacts work capacity and cognitive development. Zinc deficiency results in stunted growth. Pregnant and lactating women are also at risk for these deficiencies, and if these are not corrected, they may be passed on to the infant. Thus, generational malnutrition is propagated in similar ways as poverty throughout the world.

Pre-formed vitamin A (predominantly as retinyl esters) is obtained from animal-source foods and supplements that are not readily consumed by everybody. These foods include eggs, dairy products and liver. Provitamin A carotenoids are obtained from orange and yellow fruits and vegetables and green leaves. The major provitamin A carotenoids are alpha carotene, beta-carotene and beta-cryptoxanthin. In most tropical countries, these types of plant foods are available, albeit sometimes seasonally, but are not consumed by everyone in quantities that can promote adequate vitamin A status. Also, plant foods are not necessarily promoted at the community level because of the perceived poor bioavailability of the carotenoids according to many nutrition and public health professionals.

Two forms of dietary iron are found in foods - heme and nonheme. Heme iron is derived from haemoglobin, the protein in blood that delivers oxygen throughout the body. Heme iron is found in animal foods that originally contained haemoglobin, such as red meats, fish, and poultry. Iron in plant foods, such as lentils and beans, is in the nonheme form. Nonheme iron is sometimes added to foods as a fortificant. Heme iron is absorbed better than nonheme iron, but most dietary iron is nonheme iron. Vegetarians essentially obtain most, if not all, of their iron needs through nonheme sources. Consuming vitamin C sources like citrus fruits along with the iron source can enhance iron absorption.

Red meat and poultry provide the majority of dietary zinc to omnivores. Other good food sources of zinc include beans, nuts, some seafoods, whole grains, and dairy products. Zinc absorption is greater from a diet high in animal protein than from a diet rich in plant proteins. This is sometimes because of the presence of phytates in plant foods such as whole grains, cereals, and legumes, which can decrease zinc absorption.

## **Approaches to alleviate micronutrient deficiencies**

In developing countries, supplementation efforts often prevail over food-based approaches in the attempt to conquer nutrient deficiencies. In the matter of conquering vitamin A deficiency, vitamin A supplementation does make a difference in child health. In fact, a meta-analysis of eight studies showed a 23% reduction in childhood mortality<sup>2</sup>. However, supplementation

programmes require recurrent costs each year, and include not only the supplements but human resources also, for distribution and monitoring of the programmes<sup>3</sup>. Iron fortification may be more cost-effective than supplementation<sup>4</sup>, but supplementation has a larger impact on population health. Zinc fortification has been carried out in the United States since 1970 and has been proposed in staple foods such as rice, wheat and maize and in condiments such as salt<sup>5</sup>. However, widespread adoption of these proposals has not occurred. Supplementation and fortification approaches require constant resource allocation. Public health officers are often faced with making difficult decisions when budgets are stretched across several health initiatives.

### **Food-based approaches for combating micronutrient undernutrition**

Biofortification of staple crops with provitamin A carotenoids, iron and zinc, is an emerging and sustainable way to improve the micronutrient status of populations<sup>6</sup>, but it still cannot replace the importance of a diet rich in fruits and vegetables. Based on data in animal models and humans, biofortification with provitamin A carotenoids and iron can make a difference in the nutritional status of populations that adopt these biofortified varieties. In some instances, biofortified crops that have invisible traits will be more easily adopted than those with visible changes. For example, as long as high-zinc wheat varieties have similar agronomic traits to locally grown varieties, they may be quickly adopted because there is no behaviour change expected on the side of the consumer. On the other hand, it will take more nutrition education for a mother who has eaten white maize her entire life to adopt an orange variety with more provitamin A activity. Perhaps efforts could begin by promoting the improved varieties as more nutritious for her children during the weaning process.

As developing countries move along the income continuum, nutrition education efforts need to be in place to promote the daily consumption of low-cost, locally grown fruits and vegetables. Unlike calorically dense staple foods and snacks, the number of fruits and vegetables consumed can always be increased without substantially increasing energy intake. Efforts should continue to increase community consumption. This can occur along with supplementation and biofortification efforts.

### **Advantages of using food-based approaches to conquer micronutrient deficiencies: emerging research with vitamin A**

Vitamin A<sub>2</sub> is an analogue of vitamin A with an extra double-bond in the 3, 4 position of the ring part of the molecule, and is found naturally in fresh-water fish such as *Wallago attu*. Much of the early work with vitamin A<sub>2</sub> was performed in India<sup>7</sup>. Vitamin A<sub>2</sub> has been used as a tracer for vitamin A in fur seals<sup>8</sup>, rats, swine<sup>1</sup>, and humans<sup>11</sup>. In a study performed in piglets, vitamin A<sub>2</sub> was administered to see what the short-term uptake would be in crucial extrahepatic organs, that is, the adrenal glands, kidney, lung and spleen<sup>12</sup>. After a meal or supplement, vitamin A travels through the lymph into the general circulation in chylomicra. When the chylomicron remnants reach the

liver, vitamin A is complexed with retinol-binding protein and secreted into the blood. In this study, the piglets were killed 4 hours after dosing, and the minimum estimated chylomicron contribution to tissue vitamin A<sub>2</sub> was estimated to be 63 – 280% higher than the maximum vitamin A<sub>2</sub> exposure from retinol-binding protein in the serum. In the same study, vitamin A supplements were given to the piglets (10 days prior to killing them) at the same dosage levels as those administered to infants less than 1 year of age in developing countries, that is, 25,000; 50,000; and 100,000 IU in the form of retinyl acetate dissolved in corn oil. The retinol concentration in kidney and adrenal glands responded to vitamin A treatment, but there was no difference in the concentrations between the supplemented groups. In other words, more was not better. Furthermore, lung and spleen did not have elevated levels 10 days after treatment. It follows, therefore, that the chylomicron contribution to these essential tissues after meals containing vitamin A is important for maintaining concentrations.

Spleen and lung are active in the immune response<sup>13, 14</sup>, and vitamin A plays an integral role in immunity. Any initial storage of vitamin A that occurred in these tissues may have been utilized before sampling 10 days after dosage. The spleen is involved in both innate and adaptive immune processes in humans<sup>14</sup>. The lung has constant exposure to the environment and is one of the first defences against inhaled antigens<sup>14</sup>.

The ratio of vitamin A<sub>2</sub> to “normal” vitamin A was much higher in these two tissues than in the kidney or serum. Vitamin A<sub>2</sub> was rapidly taken up by these tissues from the chylomicra, and initial stores of vitamin A from the dose given 10 days earlier were low. If these two essential immune system organs need a constant supply of vitamin A from the diet or supplements for their proper functioning, current practices of periodic supplementation to children may not be optimal. Although few dispute the benefits of vitamin A supplementation to preschool children in preventing mortality and overt vitamin A deficiency<sup>2</sup>, food-based approaches to the global vitamin A problem need to be encouraged<sup>15</sup> alongside of supplementation programs to mitigate morbidity and maintain optimal health.

Thus, the major advantage of food-based approaches is that they allow a constant supply into the body through normal metabolic processes. Another major advantage is that the potential for hypervitaminosis is alleviated<sup>15</sup>, which may occur acutely with supplementation and chronically through fortification with preformed vitamin A. Furthermore, in the case of iron-biofortified rice fed to women, the women who benefited the most were those in whom the body reserves of iron were the most depleted<sup>16</sup>. The body's regulatory processes more easily protect against excess when the nutrients come through the food.

### **Benefits beyond basic nutrition: functional foods**

Functional foods are foods that have health benefits beyond basic nutrition. Although carotenoids are not considered to be nutrients, they are antioxidants that can quench singlet oxygen and trap peroxy radicals<sup>17</sup>. The primary carotenoids that circulate in humans are  $\alpha$ - and  $\beta$ -carotene, lycopene,  $\beta$ -



cryptoxanthin, lutein, and zeaxanthin. Of these, lycopene is the most biologically potent antioxidant<sup>18</sup> having twice the activity of  $\beta$ -carotene and ten times that of  $\alpha$ -tocopherol. In India, red carrots are commonly consumed. Red carrot not only contains bioavailable  $\beta$ -carotene for vitamin A but also lycopene<sup>19, 20</sup>. Numerous studies have examined the association between lycopene and chronic diseases such as cancer and cardiovascular disease<sup>21, 22</sup>; the pathogenesis of both may be attributed to oxidative damage. The promotion of red carrot as a functional food may be a sustainable whole food-based approach<sup>3</sup>, providing other health benefits in addition to resolving the sequelae of vitamin A deficiency. Because dietary sources of lycopene are few, and the red carrot offers bioavailable  $\beta$ -carotene and lycopene, it is a potential functional food, similar to tomato<sup>24</sup>, and can play a role in preventing both nutritional deficiency and chronic disease in carrot-consuming countries.

With regard to bone health, lycopene can inhibit mineral resorption by inhibiting osteoclast formation and the production of reactive oxygen species produced by osteoclasts to reduce the burden of free radicals in the body<sup>25</sup>. Additionally, lycopene was shown to stimulate proliferation and cell differentiation in a human cell line with osteoblastic properties<sup>26</sup>. Thus, lycopene might favourably alter bone remodelling by stimulating bone formation and inhibiting resorption. Similarly,  $\beta$ -cryptoxanthin was shown to stimulate bone formation and inhibit bone resorption *in vitro*<sup>27</sup>. In cultured rat femoral tissue,  $\beta$ -cryptoxanthin produced an increase in calcium content and alkaline phosphatase activity<sup>28</sup>. Furthermore, oral administration to ovariectomized rats prevented bone loss<sup>29</sup>.

In a recent study in postmenopausal women, serum lycopene was significantly lower in women with osteoporosis than in those without, despite there being no difference in lycopene intake. Interestingly, beta cryptoxanthin serum concentrations in the women with osteoporosis were lower than in the normal group, even though their dietary intakes were significantly higher<sup>30</sup>. Thus, the levels of carotenoids that may have beneficial skeletal effects are lower in women with osteoporosis. A higher intake of carotenoid-containing fruits and vegetables may be protective against osteoporosis.

Over the past decade, several epidemiological and clinical studies have suggested that carotenoid consumption is associated with a lower risk of cardiovascular diseases, eye diseases and of cancers, especially those of the lung, oral cavity, pharynx, prostate and uterine cervix<sup>31</sup>. However, intervention trials with pharmacological doses of isolated  $\beta$ -carotene have shown either no effect or harmful effects on lung cancer risk among smokers. This suggests that other carotenoids or components in fruits and vegetables may be responsible for the protective influences observed in epidemiological studies. Thus, the overall evidence suggests that diets high in fruit and vegetables are important for overall health and reduced risk of disease, and carotenoids are one of several components that offer health benefits.

## Summary

Across all income and education levels, healthful eating can be improved through the consumption of more fruits and vegetables. It is our duty as

nutrition practitioners to do our part for the international agenda of diversifying diets. In many countries, the income gap continues to widen and, as a consequence, so does the gap in nutritional adequacy and health status. In order to elicit change, it is of paramount importance to help the current generation of nutrition and dietetics students understand the nutritional benefits of a diet rich in fruits and vegetables. The scientific literature supports the benefits of whole fruits and vegetables in the prevention of disease. Fruits and vegetables should be considered natural functional foods, both for alleviating nutritional inadequacies and promoting general well-being.

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# NUTRITIONAL UROLITHIASIS: EMERGING MESSAGE

Teotia<sup>1</sup>SPS and Teotia<sup>2</sup> M

## Introduction

Prevalence of kidney stones is affected by genetic, environmental, and nutritional factors<sup>1</sup>. Because it appears that peaks of stone disease always occur during periods of affluence, and stone episodes are rare during war and recession<sup>2</sup>, several authors<sup>3</sup> have concluded that nephrolithiasis is -at least in part- a nutritional disease. Another hint that nutrition may be an important determinant of stone formation comes from the clinical presentation of stone disease. Whereas small upper urinary tract stones consisting of calcium oxalate or uric acid usually form in individuals living in the affluent countries, large struvite stones (mainly vesical) are most prevalent in developing countries where malnutrition, consumption of cereals (as staple food) and recurrent infections are common. On the other hand, a recent survey in India Teotia and Teotia<sup>4</sup> showed cases of vesical stones dropped sharply from 25% in 1970<sup>5</sup> to less than 3% in 1990, with increase in calcium oxalate stones and disappearance of ammonium urate stones. This makes nutritional aspects important in the studies of stone formation. This article reviews the current status of the impact of nutrition in the formation and recurrence of kidney stones.

## Fluid and water intakes

Logic dictates that increased fluid intakes raises urine volume and reduces urinary super saturation, thereby reducing the driving force for crystallization and stone formation. Low urine volume thus, must be seen as an independent risk factor for stone formation. Indeed stone incidence exponentially increases below urine volumes lower than 1.2 liters per day<sup>6</sup>. In a large cohort prospective study, the relationship between the use of 21 different beverages and the risk of stone formation was examined<sup>7</sup>. Whereas most beverages decreased the risk of stone formation, use of apple juice and grapefruit juice was associated with an increased stone risk for reasons that remain unclear<sup>8</sup>. Overall, it appears that the quantity of fluid consumed is much more important than its composition<sup>10</sup>. This has been recently confirmed by two large epidemiologic studies<sup>11</sup> where the risk of stone formation was inversely related to fluid intake. It is interesting that for many centuries, high fluid/water intake was the only existing therapeutic measure used for prevention of kidney stones<sup>1</sup>.

## High urine volume

The first prospective study ever performed, on two communities in Israel demonstrated that the incidence of kidney stones in the community aimed at

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increased fluid intake was significantly lower than in the other community where no specific advice had been given on fluid intake. In the only randomized trial from Italy<sup>12</sup> in a 5 year follow-up, the patients with increased water intake to at least 2 liter per day experienced a recurrence rate of 12%, compared with 27% in the group without specific measures and the time interval until recurrences occurred was significantly longer in patients on high water intake. This epidemiologic evidence proves that high fluid intake is the most important measure for the prevention of calcium stone recurrences.

## **Calcium stones**

### ***Calcium and oxalate***

Historically much more emphasis has been put on hypercalciuria than on hyperoxaluria, partly because reliable measurements of oxalate in biological fluids have become available only recently, whereas calcium measurements have been available for several decades<sup>13</sup>. The clinical consequence is that even slight increases in urinary oxalate are much more relevant for crystallization and stone formation than respective rises in urinary calcium<sup>14</sup>.

### ***Low calcium versus high calcium intake***

A major turnabout happened when two large prospective epidemiologic trials<sup>8,11</sup> clearly indicated that the risk for forming a kidney stone decreased with increasing dietary calcium intake. This resulted in much "confusion and consternation among patients with kidney stones and their doctors"<sup>15</sup>, however, the findings were straightforward. Compared with subjects in the lowest quintile group of calcium intake, the reduction in the relative risk for kidney stone formation in the highest quintile group was 44% in men<sup>8</sup> and 35% in women<sup>11</sup>.

Very recently, these epidemiologic data were confirmed by a randomized prospective trial over 5 years<sup>16</sup>. The driving force for crystallization, that is urinary calcium oxalate super saturation, declined in all patients over the whole study period, but was consistently lower in hypercalciuric male stone formers randomized to a diet restricted in animal protein and salt but with a normal calcium content (1200 mg per day), compared with patients consuming a traditional low calcium diet (400 mg per day of calcium)<sup>16</sup>. More important, the relative risk for a stone recurrence in patients on the normal calcium/low animal protein/low salt diet was reduced by 51% compared with stone formers on the low calcium diet. Unfortunately, the effects of the two study diets on urinary citrate were not elucidated. The most likely reason why stone recurrences are more frequent on a low calcium diet is reciprocal hyperoxaluria, which is increased intestinal oxalate absorption caused by reduced binding of oxalate by the low calcium content of the diet<sup>17</sup>.

Further studies indicated that increases in urinary oxalate carry the greater risk for crystal aggregation of calcium oxalate than increases in urinary calcium even in nonstone formers and very large amounts of oxalate can be tolerated if they are bound at the intestinal level by high amount of calcium

that is ingested simultaneously<sup>18</sup>. It therefore appears more appropriate to first advise patients on a sufficient calcium intake simultaneously ingested with food in order to avoid increases in urinary oxalate excretion. Nevertheless, efforts to restrict dietary oxalate should also be made, because they also can be effective to limit the degree of calcium-oxalate interaction in the bowel. Indeed, a recent study demonstrated that urinary oxalate does not increase, even on a low calcium diet, when oxalate is restricted simultaneously<sup>20</sup>. Overall, available evidence indicates that a low calcium diet as a treatment of recurrent calcium nephrolithiasis should be abandoned, because it may increase the number of stone recurrences and carries the risk of osteopenia and/or osteoporosis.

Despite evidence that severe dietary calcium restriction may no longer be appropriate, the controversy over the role of moderate dietary calcium restriction continues. The hardness of drinking water, for obvious reasons, has been suspected to be of importance for regional variations in the incidence of stones. In the large epidemiologic survey Teotia et al<sup>21</sup>, found a relationship between the incidence of renal stones in India and the chemical composition of the drinking water. Theoretically, hard water, which contains large amounts of calcium and magnesium, is protective against stone formation by combining in the intestine with dietary oxalate. However, hardness of drinking water may be considered as a possible contributory factor for stone formation in agricultural labour, who is working under sunshine in the summer weather for prolonged hours with excessive sweating and drinking large quantities of hard water. In this situation, the chronic dehydration and low urine volume may increase the propensity to form a stone, especially if the intake of dairy products is also high<sup>21, 22</sup>.

### ***Animal protein and sodium***

Epidemiologic data demonstrates a strong positive correlation between the incidence of calcium and/or uric acid stones and consumption of animal flesh protein<sup>2</sup>. Conversely, vegetarians have a low prevalence of kidney stones<sup>23</sup>. Biochemically a high animal protein diet (meat, fish, poultry) as consumed in many affluent communities, lowers urinary pH, decreases urinary citrate excretion, and increases urinary excretions of calcium, oxalate, and uric acid<sup>24</sup>. The acid load implemented with high amounts of animal protein decreases renal tubular reabsorption and imposes an additional risk for negative calcium balance and osteopenia, since urinary calcium excretion rises further<sup>23, 24</sup>. In addition, chronic over consumption of flesh protein may increase renal mass and thereby up-regulate calcitriol production<sup>25</sup>. This contributes to hypercalciuria by down-regulating parathyroid hormone secretion with subsequent reduction in renal calcium reabsorption<sup>25</sup>. A high sodium intake, often connected with high protein consumption, contributes to hypercalciuria, since high sodium intake reduces renal tubular reabsorption of calcium<sup>24</sup>.

In the large epidemiologic study by Curhan et al<sup>8,11</sup>, showed a significant association of formation of new kidney stones with high animal protein intake but no association with sodium consumption<sup>8</sup>. Conversely, stone formation in

women was hardly associated with protein intake, but significantly related to sodium consumption. In the first prospective randomized trial Hiatt et al<sup>26</sup>, found that after a mean follow-up of 3.4 years, stone patients on a low protein, high fiber diet (56-64 g of protein/day, wheat bran supplements) had an almost 6 fold higher risk of stone recurrence than control stone formers only instructed on fluid and adequate calcium intake (~500 mg/day). This study, however, had severe limitations. The most recent randomized trial by Borghi et al<sup>27</sup>, however, clearly demonstrates that, compared with patients on a traditional low calcium and unrestricted protein intake, stone recurrences are significantly less frequent in patients on normal calcium intake combined with reduced intakes of animal protein (52 g/day) and salts (50 mmol/day).

### **Citrate**

Low urinary citrate excretion is an accepted risk factor for calcium nephrolithiasis, because it reduces urinary super saturation by complexing calcium ions. In addition, it inhibits growth and aggregation of calcium oxalate and calcium phosphate crystals<sup>8</sup>.

### **Uric acid stones**

As in other stones, the risk of uric acid stone formation also increases with increasing urinary supersaturation with respect to uric acid. About 50% of uric acid stone patients have a fasting urine pH below 5.0, sometimes reflecting excess intake of acid containing food such as animal protein<sup>29</sup> and are therefore at risk for exaggerated uric acid crystallization and stone formation. In addition, uric acid excretion rises linearly with increases in purine intake<sup>30</sup>. A low purine<sup>31</sup> and low animal protein diet<sup>32</sup> significantly reduces urinary uric acid excretion.

### **Cystine stones**

Cystine has a poor solubility (about 200 to 300 mg/l) that increases gradually with rising pH to 7.5. Above a pH of 7.5, solubility increases profoundly and may exceed 500 mg/l<sup>33</sup>. Metabolically, methionine is a precursor of cystine, and a rigorous low-methionine diet has been demonstrated to significantly lower urinary cystine excretion<sup>34</sup>.

### **Conclusion**

Nutrition has to be regarded as a highly important additional risk factor in subjects who are prone to develop stones. Dietary excesses simply act as a tinderbox, which only in association with underlying abnormalities can lead to the hazard of stone formation.

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# INDICATORS FOR NUTRITION IMPROVEMENT PROGRAMMES AT NATIONAL AND COMMUNITY LEVELS: LESSONS FROM SOUTH ASIA

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## Introduction

Improving the nutritional status at individual, household and national levels is one of the widely agreed objectives of many international conferences and summits held in the last decade. The FAO's latest estimates of the number of undernourished people confirm an alarming trend in the context of efforts to bring about reduction in hunger in the developing world. In 2001 -2003 there were still 854 million undernourished people worldwide, of which 820 million were in the developing countries, 25 million in the transition countries and 9 million in the industrialized countries. The rate of reduction of undernutrition has slowed to a crawl and in most regions the number of undernourished is actually growing<sup>1</sup>. With soaring food prices, the adverse effects on food security and nutrition are likely to be profound.

Asia is the world's largest and most populous continent with a population of almost 4 billion people, representing >60% of the world's total population. It also has a population density (89 persons/sq. km) which is the highest in the world, more than 4 times that in North or South America and 3 times that in Africa. Among the Asia-Pacific regions, South Asia is the most populous, with a population density (461/sq. km) which is about 4 times higher than in South-East Asia and twice that of East Asia<sup>2</sup>. In relation to child malnutrition, South Asia's rank is somewhere near the middle in worldwide terms, and nutrition improvement has not correlated with the economic progress that has occurred in the last two decades. Though growth has acted as a powerful driving force for poverty reduction in South Asia, the same is not true for improvement in nutritional status. This paper provides:

- an overview of the magnitude and nature of food security and the nutrition situation in South Asia,
- the pattern of food consumption and availability;
- development indicators;
- information systems for nutrition improvement programmes at national and community levels; and
- policy considerations.

## Magnitude and nature of food security and nutrition

Virtually no progress has been made towards the World Food Summit (WFS) target of halving the number of undernourished people by the year 2015. Since 1990 -92, the baseline period for the WFS target, the undernourished

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population in the developing countries has declined only by 3 million from 823 million to 820 million. This means that the average annual decrease since the Summit has been far below the level required for reaching the WFS goal of halving the number of undernourished people by the year 2015. It also means that the rate of reduction would have to be accelerated to 24 million per year, almost 10 times the current pace, in order to reach that goal. Progress over this period was slower than over the previous two decades when prevalence of undernutrition declined by 9% (37% to 28%) between 1969 -71 and 1978 -81 and by a further 8 percentage points (to 20%) between 1978 -81 and 1990 -92. In Asia (where China and India are treated as separate sub-regions in view of their large populations) significant progress in reducing the number of undernourished people was made in China and in the most populous sub-region, Southeast Asia. In India, on the hand, though the prevalence of hunger declined, the outcome in terms of reduction in the numbers of undernourished has been small, as reduction in the first part of the decade (1990 -92 to 1995 -97) was subsequently reversed. During the same time period, the number of undernourished people increased in the rest of East Asia excluding China, and particularly in the rest of South Asia excluding India <sup>3</sup>.

### **Undernourishment and poverty**

Measures of food deprivation, nutrition and poverty are strongly correlated. While poverty is an important cause of hunger, hunger can also be a cause of poverty. Hunger deprives impoverished people of the strength and skills to work productively. Studies have confirmed that hunger seriously impairs the ability of the poor to develop their skills and reduces the productivity of their labour. Studies in children have also shown that intermittent experiences of food insecurity and hunger are associated with impaired school performance, tiredness, absenteeism and higher levels of hyperactivity in children<sup>4</sup>. Micronutrient deficiencies can also reduce work capacity. Children with anaemia are not able to concentrate and have less energy for play and exploratory activity. In adults, anaemia diminishes work capacity and productivity by as much as 10-15 %. In pregnant women, anaemia substantially increases the risk of death in childbirth, accounting for up to 20 % of maternal deaths in Asia and Africa<sup>5</sup>.

### **Pattern of food consumption and availability**

Given the multi-faceted nature of food security and nutrition, it must be agreed there can be no single indicator for measuring it, but that a variety of indicators are needed to capture the various dimensions of food insecurity. Food consumption and food consumption patterns are also determined by whether people have economic access to food. By and large, in poor countries, not only quantity of food consumed but the quality too is inadequate. Diets are not balanced, with a predominance of relatively low-cost cereals and few high-value food items, particularly foods of animal origin, vegetables and fruits. Malnutrition is therefore a common feature in these countries, especially among women and growing children whose food and nutrient needs are relatively higher than those of the other population groups<sup>6</sup>.

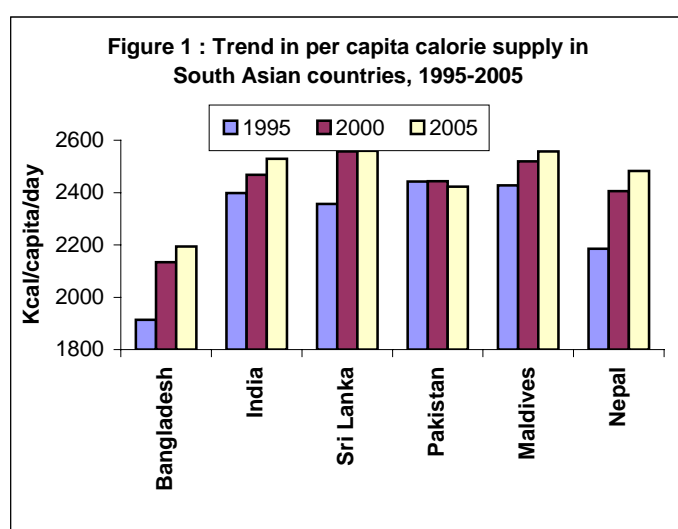
## Food consumption patterns in South Asia

South Asia comprises seven countries including Bangladesh, Bhutan, India, Nepal, the Maldives, Pakistan and Sri Lanka. South Asia is the poorest region of the world next to sub-Saharan Africa in terms of all measurable development indicators. As a region it is home to approximately 23% of the world population, yet, in 2005, over one-third of the world's poor and undernourished persons lived in this region, (estimated based on the internationally comparable poverty line of 'one dollar a day in 1985 purchasing power' and a calorie consumption line of 2100 kcal/person/day)<sup>1</sup>. Although there are many commonalities among the countries of the region, considerable differences exist among them in terms of agricultural and economic development and other human development indices<sup>1, 7,8</sup>. These differences arise due to (among other variables) differences in the food security and food supply situations in these countries.

## Food supply situation and nutrition

Every year, the Food and Agriculture Organization of the United Nations (FAO) prepares Food Balance Sheets of countries of the world from where data on food production, import (commercial, food aid), export, feed and seed and other net uses (industrial and other) are available. The net supply of food available for human consumption is calculated from (production + import) – (export + feed and seed + other net uses). Data thus obtained for food for human consumption concurs fairly well with actual intake data obtained from household food consumption surveys and is thus a dependable proxy indicator of food consumption patterns in a given country. Food Balance Sheets are displayed in the form of both quantity (total and per capita per day) and kilo calories (kcal) (total and per capita per day)<sup>9</sup>. In this paper, all data are shown as kcal/capita/day for each food item.

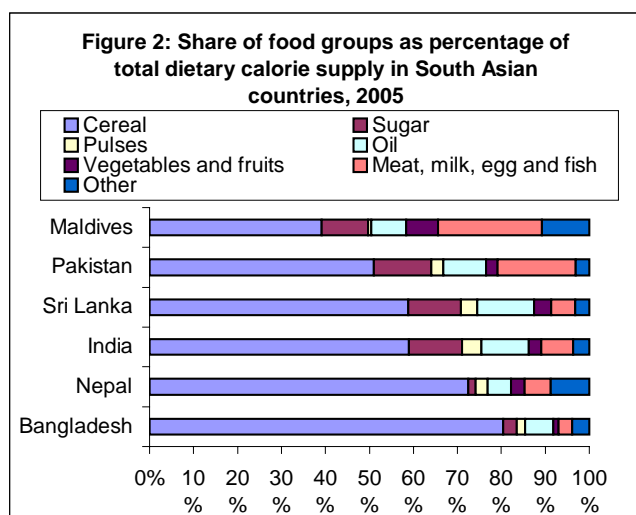
Country	Kcal/capita/day
Bangladesh	2200
Pakistan	2320
Sri Lanka	2390
Nepal	2430
India	2470
Maldives	2600
South Asia	2424



Information on per capita energy availability calculated by FAO provides a picture of the patterns of food consumption and food security in some of the countries of Asia<sup>10</sup>. Using 2002-2004 data, Table 1 gives the dietary energy supply in countries in South Asia. Maldives had the highest national per capita dietary energy supply (2600 kcal/day), while Bangladesh had the lowest

(2200 kcal/day).

Overall, the average dietary energy supply in South Asia is 2424 kcal/capita/day. Analysis of the trends in dietary energy over the ten years between 1995-2005 shows that the per capita energy supply in all countries except Pakistan has increased during this period, with Bangladesh and Nepal, the two poorest countries, improving their per capita calorie supply by about 300 kcal each, Sri Lanka by 200 kcal, India by 130 kcal and Maldives by about 100 kcal. The energy supply in Pakistan remained static at the level of just over 2400 kcal/capita/day during this period (Figure 1).



The share of food groups as percentages of the total dietary calorie supply is an indicator of dietary diversification in South Asian countries, and is shown in Figure 2. The figure shows that Bangladesh has the highest dietary energy supply from cereals (DES Cer %, an indicator of poverty), amounting to 80%, followed by Nepal, 72%. The lowest DES Cer % is in Maldives (39%). A high intake of sugar, which is a characteristic feature of the

changing dietary trends in Asia, is noted to be approximately 12% in India, Sri Lanka, Pakistan and the Maldives, compared to only 3% in Bangladesh and less than 2% in Nepal. Sri Lanka has the highest consumption of edible oils (12.9% of total energy, mostly as coconut oil), followed by India (10.8%, all types) and Pakistan (9.7%, mostly palm oil). The Maldives and Pakistan consume the highest percentages of foods of animal origin (23.6% and 17.7% of the total energy, respectively) in the region, as compared to the minimal contribution made by foods of animal origin to diets in Bangladesh (3.1%). Diets in the Maldives have relatively higher percentages of fruits and vegetables (7.3% of the total calories), as compared to only 2.6% in Pakistan and less than 2% in Bangladesh. This reflects the poor diversification of the diets in Bangladesh and Nepal. The diets in other countries are relatively more diversified.

There are notable differences among the South Asian countries in the types of cereals and other food products consumed. For example, rice is by far the most predominant cereal in Bangladesh whereas wheat takes predominance in Pakistan. The other countries consume both rice and wheat, with more of rice than wheat. As for foods of animal origin, Pakistan has the highest consumption of milk in the region, while Maldives consumes most of its animal foods in the form of fish. Beef is the largest component of the meat consumed in Pakistan and Nepal, whereas in Sri Lanka and the Maldives more chicken is consumed as compared to other meat products. In respect of

fish, Bangladesh and Nepal consume mostly fresh water fish while in Sri Lanka and the Maldives marine fish are predominantly consumed.

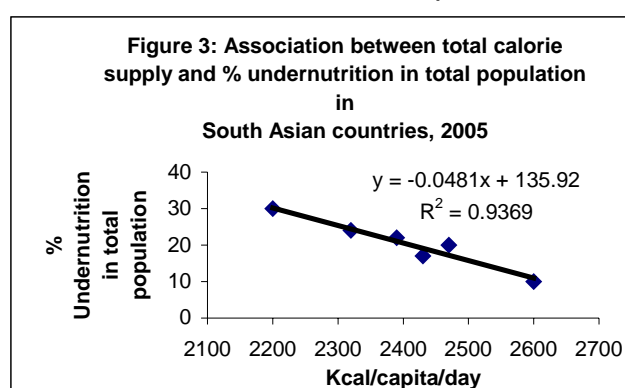
The quantity and quality of diets in a country are a clear reflection of the nutritional status of its population. Table 2 shows the prevalence of undernutrition in the total population and stunting and underweight among under-five-year-old children in South Asian countries.

Country	Under nutrition (Total population)	Stunting (U5 population)	Underweight (U5 population)
Bangladesh	30	43	48
India	20	46	47
Sri Lanka	22	14	29
Pakistan	24	37	38
Nepal	17	51	48
Maldives	10	25	30

The prevalence of undernutrition in the total population is highest in Bangladesh (30%) and lowest in the Maldives

(10%); other countries have undernutrition figures ranging from 17% to 24%. Bangladesh, India, Nepal and Pakistan experience high prevalence of under-5 stunting, and the incidence of underweight ranges between 43% - 51% and 47 - 48%, respectively. Sri Lanka has the lowest incidence of child stunting rate (about one-third that in Bangladesh, India and Nepal, and one-half that in the Maldives). Sri Lanka and the Maldives have similar rates of prevalence of underweight in children.

One-way ANOVA test of the data from the South Asian countries shows that total per capita energy supply is significantly ( $r^2 = 0.937, p = 0.001$ ) negatively associated with the percentage of undernutrition in the total population (Figure 3). There is also a positive, although insignificant ( $r^2 = 0.511, p = 0.110$ ), association between national income and total per capita energy supply (data not shown). Thus, national income largely, but not wholly, determines the pattern of food consumption and nutrition in a country<sup>11</sup>.



### Development indicators

Table 3 shows some of the development indicators for South Asian countries, having a bearing on the food security and nutrition situation. In South Asia, the most populous countries in terms of density of population are Bangladesh (1045/sq. km) and the Maldives (1104/sq. km). Bhutan has the lowest population density (46/sq. km). The Maldives is the richest country in the region, with per capita Gross National Income (GNI) of US\$2680, followed by Bhutan (US\$1410) and Sri Lanka (US\$1300). Nepal has the lowest GNI (US\$290), with Bangladesh coming in at one rank above (US\$480) (Table 1).

**Table 3: Some characteristics of South Asian countries<sup>11</sup> Source: FAO RAP (2007);  
<sup>2</sup> 2005 data; <sup>3</sup> 2006 data.**

Country	Population density (per sq. km) <sup>2</sup>	Per capita GNI (US\$) <sup>3</sup>	Life expectancy at birth (years) 2005-2010		Infant mortality rate (per 1000 live births) <sup>1</sup>
			Male	Female	
Bangladesh	1045	480	63.2	65	54
India	336	820	63.2	66.4	56
Maldives	1104	2680	67.6	69.5	33
Nepal	184	290	63.2	64.2	56
Pakistan	198	770	65.2	65.8	79
Sri Lanka	316	1300	68.8	76.2	12
Bhutan	46	1410	64	67.5	65

Sri Lanka and the Maldives have the lowest IMR (12 and 33, respectively per 1000 live births) and the highest life expectancy at birth (68-69 years for men, 70-76 years for women) in the region. These two countries also have the highest HDI (Human Development Index) scores, 0.743 and 0.741, respectively. Bangladesh and Nepal have the lowest HDI scores. The data also show that the Maldives, although having a GNI twice that of Sri Lanka, has three times the incidence of IMR. Thus, health indicators such as IMR are not always in close correspondence with national income.

### Information systems for assessing food insecurity and vulnerability

The FAO's Food Insecurity and Vulnerability Information and Mapping Systems (FIVIMS) framework provides a range of activities that can be carried out, both at the national and international level, in support of improved information to achieve the goals of food and nutrition security. At the national level it is implemented through a linking of information systems that gather and analyze data relevant for measuring and monitoring food insecurity and vulnerability<sup>12</sup>.

#### Categories of existing national information systems and indicators

Most countries have established statistical services and systems that generate and analyze information. Some categories of existing national information systems include those dealing with agriculture, health, land, water and climate, early warning systems, household food security and nutrition information systems, market information systems and vulnerability assessment and mapping systems<sup>13</sup>. Examples of a set of key food and nutrition indicators that are relevant to food security and nutrition are given in Box 1

#### Box 1: Food and nutrient intake indicators

- Average energy intake
- Average food intake of major groups
- Daily per caput protein intake
- Percentage of energy from protein
- Daily per caput carbohydrate intake
- Percentage of energy from carbohydrate
- Daily per caput fat intake
- Percentage of energy from fat
- Percentage of protein from animal source
- Dietary energy supply
- Percentage of undernourished population

At the national level, strengthened and more integrated food insecurity and vulnerability information systems will provide better and more up-to-date

information to the policy makers and members of civil society concerned with food security issues at all levels in the country, and will facilitate the assessment of policy and programme options for improving the nutrition situation. The focus of most information collection and analysis is by sectoral or sub sectoral units. Technical constraints are generally found to arise from lack of trained human resources to manage complex information systems and conduct the multi-sectoral analyses that are required for tackling food security issues. The best method of measuring household food security is another issue of much debate, partly because of the cross-linking areas of food security and nutrition issues<sup>14</sup>. For example, in terms of data use, it is recommended that, in food consumption surveys, the weighed food method or the 24-hour dietary recall method should preferably be used. In the case of non-availability of such information, data derived from surveys on food frequency questionnaires would need to be used. It is also very important that only representative, nation-wide surveys with special emphasis on the most recent information available be used.

### **Food consumption, utilization and nutritional status: example from Orissa**

Studies of food security and vulnerability were undertaken in selected States of India as part of an FAO-supported FIVIMS India pilot project launched in 2003 by the Ministry of Food and Consumer Affairs together with the State-level departments of food and public distribution<sup>15</sup>. The study, which covered four districts in Orissa and also the State of Himachal Pradesh, assisted in the development of a framework for establishing an information system to monitor

Indicator	Orissa	India
Infant mortality rate (per 1000 live births)	65	57
% Children 0 to 3 years who are underweight	44	46
% Children 12 to 23 months who are fully vaccinated	52	44
% households using piped drinking water	10.2	42.0
% households with toilet facilities	19.3	44.5

food insecurity and vulnerability in Orissa. A vulnerability group profiling approach (VGP) was used to estimate the number of vulnerable persons, identify them and their geographical

locations, and determine the reason for their vulnerability. The VGP can be used to analyze the multiple factors influencing food insecurity in relatively homogenous groups: their assets, external factors that affect lives in the community, their own actions resulting in intermediate outcomes, and ultimate food security status. The most important criterion to identify common livelihood groups is sources of income (often closely associated with location on the basis of relatively homogenous livelihood /agro ecological zones). The VGP is a simple and relatively low-cost tool for building an overview of vulnerability and food insecurity grounded in local knowledge. The basic methodological framework covered five steps: review of existing data, identifying main vulnerable livelihoods, community level qualitative research, household level quantitative research, and validation. This tool helps to uncover the relative degree of vulnerability of different sub-groups and identifies the key characteristics of each. These include asset base (e.g. land access), geographical characteristics of physical assets, possible livelihood



strategies, diet and nutritional status. An overview of key indicators for undernutrition and health in Orissa is provided in Table 4<sup>16</sup>.

### **Food and nutrition indicators: example from Bangladesh**

An inventory through the FIVIMS initiative in Bangladesh revealed a rich information system accessed and used by various organizations – government, non-government and academic – for purposes determined by their own mandates<sup>17</sup>. Inter-sectoral analyses of child malnutrition data were collected by three organizations (Bangladesh Bureau of Statistics, Ministry of Finance and Planning which conducts the Child Nutrition Survey of Bangladesh; National Institute of Population Research and Training of the Ministry of Health and Family Welfare which conducts the Bangladesh Demographic and Health Survey, and Helen Keller International, an international organization which conducts bimonthly Nutritional Surveillance Programme (NSP). These data show a persistent decreasing trend in child stunting and underweight during the 1990s (from 60-70% in 1990 to 48-50% in 2000). The NSP however shows a slightly higher prevalence (5-10%) of malnutrition.

Data sets on maternal malnutrition from both BDHS and NSP show a high prevalence of chronic energy deficiency among women of childbearing age (40-55%) indicated by a body mass index (BMI) of <18.5 kg/m<sup>2</sup>. Data from these sources also show a decrease in maternal malnutrition during the period 1992 -2000. The latest national data show the prevalence of low birth weight to be 36 %<sup>18</sup>, that of anaemia in children under the age of five years to be 60 %<sup>19</sup>, and Iodine deficiency disorders among school age children to be 34 %<sup>20</sup>. IDD surveys are regularly being conducted every five years in Bangladesh.

### **Seasonality- and disaster-related indicators**

Selected smaller-scale surveys pertaining to a vulnerable area or a population group facing recurrent adverse conditions, seasonality or food shortages as a result of natural calamities or man-made disasters may also be included. At-risk population groups, trends and seasonal variations should especially be kept in mind when presenting food consumption data. In particular, if there is prior information to suggest that problems of malnutrition and food insecurity are concentrated in certain regions or among certain social groups, then it would be necessary to concentrate on those specific issues. There would be a need to disaggregate food consumption data as much as possible. Average food intake derived from food consumption data should provide kg/person/year by major food groups, kcal/person/day including total energy, percentage from protein and fat and, if available, also the percentage of energy by major food groups; protein and fat intakes in g/person/day including the total intakes and the percentages from animal and vegetable sources; the intake of micronutrients should also be included, if the data are reliable and appropriate. Typically, for micronutrients for which there is likely to be a high day-to-day variability in intake, food frequency questionnaires would need to be combined with multiple recalls on sub-sample populations.

## Community based assessment

Dietary modification and diversification indicators can be used to assess nutrition improvement in community-based programmes (Table 5). This approach can be used to enhance our understanding of micronutrient

Input	Output	Outcome
<u>Dietary improvement:</u> Food production for consumption; Information, Education and Communication (IEC); (FBDGs); complementary food production	<ul style="list-style-type: none"> <li>➤ Number of home gardens; number of chicken and duck raising activities; number of community fish ponds</li> <li>➤ Consumption of micronutrient rich foods (bioavailable) food combinations</li> <li>➤ Dietary intake of enhancers</li> <li>➤ Avoidance of inhibitors</li> </ul>	↑ Knowledge, Attitude and Practice (KAP) towards usage of micronutrient rich foods; ↓ micronutrient deficiency prevalence → gradual elimination major micronutrient deficiencies (IDA and VAD)
<u>Food fortification:</u> Iodized and double fortified salt; other foods	<ul style="list-style-type: none"> <li>➤ % household usage of iodized/double fortified salt; % individual and household use</li> </ul>	↑KAP towards usage of micronutrient rich foods; ↓ IDA and IDD prevalence → elimination of IDA and IDD
<u>Basic health services and community participation:</u> Antenatal Care (ANC) , immunization, parasite control, hygiene and related activities/services	<ul style="list-style-type: none"> <li>➤ Frequency of contacts with pregnant women (minimum 4 Antenatal Care contacts); % coverage of target groups</li> </ul>	Improved pregnancy outcomes (increased birth weights); ↓ IDA prevalence; ↓ worm infestation rates
<u>Agricultural extension services:</u>	<ul style="list-style-type: none"> <li>➤ Mobilizing small farmers, households, women's groups towards food production activities;</li> <li>➤ Number of poultry vaccinations carried out</li> </ul>	↑ Knowledge, Attitude and Practice (KAP) towards usage of micronutrient rich foods; increase in household income; ↓ prevalence of micronutrient deficiency → gradual elimination

deficiency in the community, and help to empower the community to be more self-reliant in addressing its nutritional problems<sup>21</sup>.

## Policy considerations

An important first step is the identification of food-insecure and vulnerable groups, the prevalence and extent of low food intake and undernutrition among these groups, and the reasons for their food insecurity and vulnerability. Such information makes it possible to monitor and assess the situation, and to design and evaluate possible policies and interventions. This is also essential for designing and directing interventions that actually reach the undernourished and vulnerable people efficiently.

Such operational activities can also provide a wide range of community-based food security and nutrition-related indicators that can be periodically re-

evaluated so as to strengthen community awareness and promote food security and assess nutritional needs at various levels. The purpose of national and community information systems is to facilitate the access by various user groups to more comprehensive information that is up-to-date and easy to interpret, so as to enhance food security policy information and improve the design and focus of interventions. The different sectors need to be linked in such community-based programmes in order to build a truly multisectoral approach. The development of policies that are strongly supportive of community-based programme implementation can greatly empower communities and improve the existing levels of food security.

## **Conclusion**

The ultimate goal of nutrition improvement programmes is to impact the target communities, and improve the lives and nutrition status of the population. Systematic management information systems at different levels, with data presented in different forms for different purposes and objectives, need to be established. Fundamental to the sustainability of programmes in a community is the ability of its members to make enlightened decisions and then be able to implement them. Many of the actions needed for achieving the objectives laid out by nutrition improvement programmes involve relatively little additional cost to governments. They entail assigning higher priority to integrated nutrition training, devolving responsibility to the district, sub-district and community levels, and carrying out the process of social mobilization for empowering the extension workers and volunteers, individuals and communities, to take action; and fostering greater inter-sectoral collaboration. What is needed is the political will to instill in the community a strong sense of ownership and strengthen capacity building along with appropriate tools to implement policies for improvement of the nutritional status of the population.

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# REFLECTIONS ON STUNTING

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## Introduction

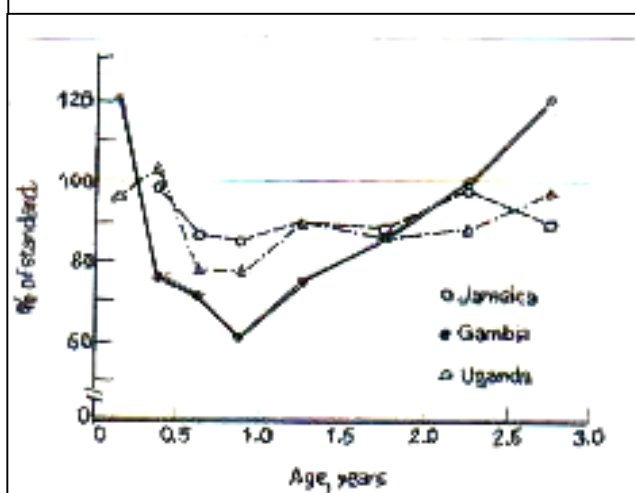
I am very glad to make a contribution to the Festschrift marking Gopalan's 90th birthday, because he has been a friend of mine for some 60 years. In 1946 I had just returned from a spell in the Caribbean, where I had been sent to investigate why so many infants and young children were dying. At that time Gopalan was studying for a Ph.D. under B.S. Platt, the Director of the Medical Research Council's Human Nutrition Unit. Many of the cases that I had seen were examples of oedematous malnutrition in children of the type described by Cicely Williams in West Africa under the name 'kwashiorkor', but that had not been previously observed in the Caribbean. I was eager to discuss my findings with Gopalan. Gopalan returned to the Nutrition Research Laboratory at Coonoor (before it moved to Hyderabad as the National Institute of Nutrition) and produced a series of papers on malnourished infants. We therefore had a strong common interest. This has been maintained in the years since then, with the emphasis gradually shifting from oedematous malnutrition to the much commoner growth failure that is implied by the term 'stunting'. This, therefore, is the topic that I shall discuss here, and it is timely to do so.

## Stunting in children

In a series of articles that appeared recently in the *Lancet*<sup>1</sup> on Maternal and Childhood Malnutrition, stunting plays a central role; world-wide, about 40% of children under 5 years of age are reported as being stunted as per the WHO definition; Gopalan has drawn attention to stunting again in a recent article in the *Bulletin of the Nutrition Foundation of India*<sup>2</sup>, It appears that, in some parts of India, approximately 50% of children below the age of 5 years are stunted. There is an enormous amount of literature on the subject, and this has been discussed in depth in an excellent review by Golden<sup>3</sup>. I shall cite only a few papers that have been keystones in my thinking.

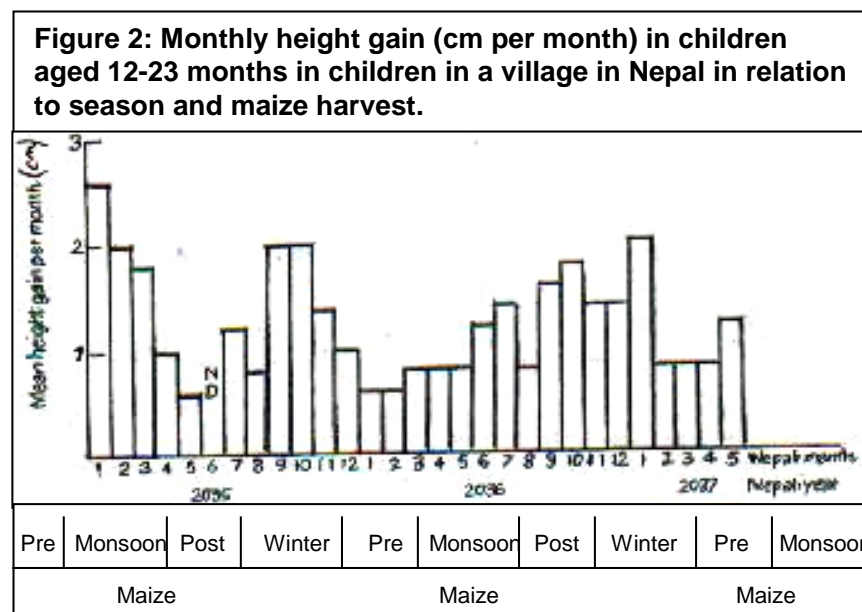
Stunting, by definition, is retardation in linear growth, and many children are already stunted by 9 months of age. As it takes some time for the process of

**Figure1: Rate of growth in length-height in infants up to 3 years, expressed as a percentage of the reference rate, in three longitudinal studies.**



*stunting* to reach the end-result of *stunted* – i.e. 2 SD or more below the mean of the WHO standard – it is useful to look at the rate of growth rather than the height attained. Figure 1, which is based on data from longitudinal studies in 3 different countries, shows that the rate of growth began to fall off soon after birth, and reached its lowest level at about 1 year of age, after which it began to climb towards the normal rate. I do not know how far the early slowing of the growth rate is related to intra-uterine growth retardation. The *Lancet* review<sup>1</sup> (Paper 2) suggests that pre- and post-natal influences make approximately equal contributions. As far as post-natal development is concerned, it is obvious that the period from 6–24 months is crucial. After about the age of 1 year the rate of growth begins to pick up, and by 3 years of age it approaches the normal rate. At puberty the growth-plates fuse, and many studies found that puberty was delayed by 1-2 years, so that the period of growth was prolonged. To reverse Gopalan's phrase, what is lost on the swings is regained on the roundabouts.

### Catch-up growth



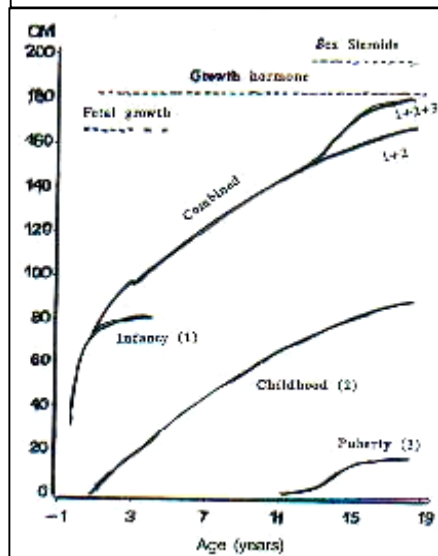
How far is complete catch-up – i.e. regaining of normal or nearly normal height – possible? For a review, see Golden<sup>3</sup>. It seems to occur in some environments, e.g. Kenya, Jamaica, South Africa and Senegal,

but in others, e.g. India and Guatemala, the growth curves are parallel from 5 years of age to puberty, with the initial deficit persisting. The most striking example of this pattern is in the data from the study of Satyanaryana et al.<sup>4</sup> in Hyderabad; in boys who were severely stunted at 5 years of age, the increase in height between the ages of 5 and 18 years was equal to that of boys in California, but the total deficit remained unaltered. It is clear that the force suppressing linear growth was operating only in the first few years of life. This was a longitudinal study of two different groups of children, stunted and non-stunted. The same conclusion can be drawn from the numerous examples of children being transferred from a poor to a good environment. The extent of catch-up seems to depend on the age at which they were transferred. Further evidence of the plasticity of linear growth in young children is the seasonal variation in growth rate that has been observed in Nepal (Figure 2) and in Bangladesh.

## Stunting as index of socio economic deprivation

Stunting has come to be regarded as an indicator of socio-economic deprivation, and the question naturally arises: does nutrition play any part in stunting, and if so, what? I am inclined to think that it does. The *Lancet* review<sup>1</sup> (Paper 3) stated that

**Figure 3: The 3-phase (ICP) growth model for height of boys. The contributions to the total, cm, are: total 179.5; infancy 79; childhood 85; puberty 15.5.**



supplementation programmes were shown to increase the height-for-age Z-score by 0.4 SD units. There are many instances, going back to the work of Boyd Orr in the 1930s, of the beneficial effects of milk, but whether these are due to any particular nutrient – protein, calcium, zinc, etc. – we do not know. My pet theory is that the crucial factor is methionine; this is based on the finding of Millward's group<sup>5</sup> that in rats a low-protein diet retarded the growth of the long bones and reduced the uptake of sulphate into the growth cartilage. Golden<sup>3</sup> also suggests this possibility. However, this hypothesis is probably far too simplistic. A very important contribution is that of Karlberg<sup>6</sup>, who proposed that the growth of a child could be divided into 3 phases that are additive – infancy, childhood and puberty. On the basis of data from studies in Pakistan he suggested that the growth curve of stunted

children could be explained by retardation of the onset of the childhood phase (Figure 3). He went on to say: "The infancy phase is nutrition-dependent, the childhood phase growth-hormone supported, and the puberty phase driven by sex steroids - a hypothesis that is supported by current knowledge in endocrinology." This statement was made 15 years ago; whether new knowledge since then supports or refutes this hypothesis I do not know, but it gets us away from the idea of stunting as the result of a purely quantitative deficiency of a single nutrient to a qualitative physiological deficiency of a particular process.

## Stunting and mental function

After the pioneering studies of Cravioto in Mexico, it is now well established that stunting in early childhood is accompanied by mental and behavioural handicaps. I am particularly impressed by the work of Grantham-McGregor and her colleagues in Jamaica<sup>7</sup>. Stunted children and non-stunted controls aged 9 months to 3 years were given supplementary food, or stimulation in the home, or both every 2 weeks for 2 years. The positive effect on growth after 2 years of stimulation was greater than that produced by food supplements, and the two were additive. The children were tested again when they were 17-18 years old, i.e. some 15 years after the original programme had ended. By this time, the stunted children had achieved considerable catch-up in height. The remarkable finding is that, even after this long 'silent'

time-interval, the stunted children who had been stimulated had achieved levels of IQ and of cognitive and educational outcome that were only a little, but not significantly, lower than those of the non-stunted control children, whereas the stunted children who had not been stimulated remained significantly behind in nearly all the tests. Supplementary feeding had no lasting effect. An important feature of this work was to show not only the long-lasting beneficial effect of early stimulation, but that this effect can be achieved by relatively untrained personnel at very little cost, so that, from the point of view of public health, stimulation of stunted children is a more practical measure than it might seem.

Retardation of skeletal and mental growth occurs together at a time of life when growth of the cerebrum and the laying down of new cells in it are particularly rapid<sup>8</sup>. Presumably the two processes, skeletal and cerebral growth, are differently regulated; the fact that they occur together means that physical stunting, of no importance in itself, should be regarded as an indicator of mental retardation. It is this that gives stunting its significance as a public health problem, and one that is essentially preventable.

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**Section – 2**

**FELICITATIONS**

## DR. GOPALAN: THE OUTSTANDING INDIAN HEALTH SCIENTIST

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*It has been my good fortune to know and be closely associated with Dr. C Gopalan for over 30 years. During this period I have developed an unbounded liking, great personal admiration and profound respect for him. I consider Dr. Gopalan to be one of the most outstanding Indian health scientists of our times. Yes – he belongs to a very select, now almost extinct tribe of scientists. Fortunately, Dr. Gopalan is still very much with us, perhaps the last of this rare tribe but still retaining much of its glitter and all of its charisma. He thinks deeply, speaks gently and softly, never minces his words when he tries to drive home his own point of view, sticks to principles and ethics and has a genuine scientific temper. At ninety, Dr. Gopalan is still as crisp and fresh in thought and action as a man half his age. When you meet him, he prefers to talk about prospects of public health in India for the future rather than his own past and his achievements. He is not a seeker of fame. He is an inspiration for all young scientists. I deem it an honour and privilege to contribute to the Festschrift being brought out to honour him.*

## **DR. GOPALAN'S SERVICES TO THE NUTRITION COMMUNITY**

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*President of the Society for Gerontological Research,  
New Delhi, India*

*The name, Dr.C.Gopalan, is synonymous with nutrition not only in India but also throughout the countries of the South East Asia Region, Asian countries, and even in countries in various other parts of the world. In fact, on the occasion of the Asian Congress of Nutrition, held a few years ago in New Delhi, it was mentioned that in any country, whenever nutrition is being discussed, the name of Dr.Gopalan would undoubtedly come up.*

*Dr.Gopalan started his career as a nutrition scientist in the Nutrition Research Laboratory (NRL), a small research institution in Coonoor, a hill township in Tamil Nadu. Within a few years Dr.Gopalan was able to make important contributions at this institution, and later it shifted to Hyderabad. Under his leadership NRL grew and developed into the National Institute of Nutrition (NIN). It become the most important centre for nutrition research not only in India and but also among the entire South East Asian countries. His spectacular work in India in the field of pellagra and many other malnutrition-related diseases is still recognized internationally. Dr.Gopalan's work in food safety, nutrition surveillance and other related areas have been recognized as being outstanding. Over the years, NIN also expanded the scope of its research activities in various nutrition-related areas like food safety, dietetics and nutrition monitoring and surveillance. When Dr.Gopalan moved to Delhi as the Director General of the Indian Council of Medical Research, he provided a major thrust to evidence-based national programmes for improving the nutrition and health status of Indians.*

*After he retired, Dr.Gopalan's expertise in nutrition was availed of by the WHO as an Advisor. In that capacity he traveled to various countries of Asia and advised their governments regarding policies and programmes in nutrition. Not content even with all these accomplishments, Dr.Gopalan established and nurtured the Nutrition Foundation of India in New*

*Delhi. The NFI is now well recognized as an influential nutrition research institution in the entire region.*

*On this happy occasion, when Dr.Gopalan reaches ninety years of age, I congratulate him for his decades of service to the field of nutrition, and hope that the nutrition community worldwide will continue to have the benefit of his wisdom for a long time to come.*

## *DR C GOPALAN AT 90: A CHERISHED LEADER OF THE MEDICAL PROFESSION OF INDIA*

*Banerji D*

*Professor Emeritus, Centre of Social Medicine and Community Health  
Jawaharlal Nehru University, New Delhi, India*

*Dr Gopalan had been twelve years older than me for many years. He and his life story had been a source of inspiration and support to me. There are hundreds of others who have had the privilege of being inspired by his life, work and direct advice and guidance. He is in line with the traditions set by B C Roy, Jeevraj Mehta, Lakshmanaswami Mudaliar and some of the top personnel of the Indian Medical Service who maintained the dignity of the medical profession. He stands out sharply today when we have been mute witness of seeing persons occupying key positions of responsibility in the medical profession making brazen compromises with their conscience and professional ethics for cheap personal gains.*

*We are also witnessing the murky drama of gruesome efforts that are being made to literally bring down a national institution, which had been nurtured with so much of care by so many eminent members of the profession over the years.*

*Gopalan had stood fast against bullying and manipulations by uninformed and arrogant politically supported bureaucrats. He also never hesitated to challenge the power of the market forces, which have often tended to distorted science and scientific findings to promote sale of their products. As a good scientist, Gopalan had been consistently raising issues concerning what can be called the political economy of the drugs and pharmaceutical industry in the country. A collection of his writings in NFI Bulletin and other journals can serve as a valuable reading material for students of nutrition science and public health..*

*Less than a year back, on September 1 2007, the EPW published his article with the very apt title, "From 'Farms to Pharmacies': Beginnings of a Sad Decline". In his characteristically forthright style, he has contended that the notion that a cocktail of synthetic nutrient, manufactured by pharmaceutical agencies, is required for a balanced*

*intake is a completely mistaken one. He uses the full force of authority of his profound and extensive scholarship in nutrition to firmly reassert that a diet of cereals, pulses, legumes, fruits and vegetables \*vegetarian!) can meet these micronutrient requirements. The totally brainwashed young, 'educated' mother, who is being constantly bombarded by sage advice of equally brainwashed 'nutrition experts about the absolute need for their darling child to consume a plethora of the so-called micronutrients, is likely to have an apoplexy if she is exposed to what could be considered as heretical views, even it comes from a person of the stature of Gopalan. Today's physicians, even the topnotch among them, simply will not be willing to listen to any contrary view, even if that happens to come from Gopalan, so much is the power of the globalised market forces.*

*Making a public health approach to nutritional problems in the country had been a major field of interest to Gopalan. He had been deeply concerned about the health of mothers and children in the country for many years. He had pointed out the dimensions of the problems by repeatedly drawing attention the vicious cycle of mothers' severe malnutrition and under-nutrition leading to similar problems amongst the children born to them. He marshaled data to show how extensive prevalence of this problem in India. Interestingly, the political leaders, who lived in well-guarded air-conditioned bungalows of New Delhi, were not amused. How can that be so, they exclaimed. They showed their crass ignorance and arrogance by asserting; 'We do not see so much of malnutrition when we visit rural areas'. It was out of question for a scholar of Gopalan's stature to 'revise' his data to placate these ignoramuses. Probably, a black dot was hoisted against his name for daring the challenge the intelligence of the chosen people.*

*True to Gopalan's deep commitment to a cause, at the age of 88, he took the initiative of organizing a Symposium on Primary Health Care: New Initiatives. The question that troubled me immediately was, why did NFI have to take the initiative when there are so many other organizations, which ought to have been interested in this subject? The term, Primary Health Care, has long been wiped out from the radar screen of public health practice by certain powerful international and national social and political forces, to make space for promoting their agendas. This leads me to my oft repeated quotation from the Czech author, Milan Kundera:*

*“Man’s struggle against oppression is a struggle between memory and forgetfulness”. We are all beholden to Dr Gopalan and the Nutrition Foundation of India for joining the fight and use their considerable stature in retrieving the “memory” of Primary Health Care in an attempt to give a new direction to promoting health and health services in India and elsewhere.*

*I also fondly recall how Dr Gopalan unhesitatingly called into question the research findings (fashionably called “evidence base”) claiming value of administration of Vitamin A in the growth of children. Dr Gopalan had gone on to explore the political economy of such manipulation of research to sub-serve interests of the drug industry. He had been equally forthright in questioning the decision of UNICEF to import very expensive weighing machines from abroad for India’s programme of growth monitoring of children. At the time of opening of the impressive building of the Nutrition Foundation of India, he had remarked that he had diligently refused to accept any financial support from the industry, governments in India and from international agencies to ensure autonomy of NFI.*

*When I was chosen by NFI to deliver the C Ramachandran Memorial Lecture for 2006, I discretely asked him whether I should tone down my criticism of some who had been supporting NFI. His response was instantaneous. He said, ‘Banerji, once we have chosen you for the Lecture, you have the full freedom to write what you think best’. That was quintessential Gopalan.*

*There might have been many references in this volume to the details of his work from many who had had closer association with him. I would merely refer to his scholastic achievements in clinical medicine; his outstanding work as a laboratory research scientist; his attaining a stature of one of the most eminent nutritionist in the world on the basis of significant work he had done in India; his landmark achievements in building the NIN and NFI and training a new generation of nutrition scientists; his capabilities as a good administrator; and, his deep social sensitivity in nutritional programme formulation.*

*I pat my tribute to this living legend.*

## **DR GOPALAN: A TOWERING FIGURE IN THE FIELD OF NUTRITION**

*Berg A*

*Guest Scholar, The Brookings Institution, USA*

*Dr. C. Gopalan has been a towering figure in the field of Nutrition for much of the past century. This was the result of his remarkably high intelligence, his forceful personality and his strong commitment to bringing about nutrition improvement. In fact, there are few people I have come across who, through their energies and dedication, have managed to put their mark on the nutrition sector the way Dr. Gopalan has. Although it was India that he served faithfully for so long, his influence has been felt internationally.*

*A world-class scientist, throughout his long career Dr. Gopalan also has been very much a pragmatist who sees the practicalities and how new ideas could be fitted into the real world. In that regard and to help bring that about, he had a unique capacity to make complex things simple. As with all civil servants, he had to submit to the regulations of the bureaucracy. He respected them but, uniquely, was not imprisoned by them. Dr. Gopalan was never afraid of taking risks. He knew how to take them with balance and wisdom. He knew how to cut through the bureaucratic mindsets to get out of the box,*

*Dr. Gopalan's career has had real meaning for so many, who valued his leadership, his inspiration and his friendship. Clearly his remarkable influence will continue to be felt deeply and widely for many years to come. Although over the years we sometimes had substantive professional differences, Dr. Gopalan always commanded my respect. I feel privileged to have crossed his path.*



## **DR GOPALAN: A GALLANT GENTLEMAN**

*Ferro-Luzzi A*

*Professor, National Institute Nutrition, Italy*

*I have always had great respect and esteem for Dr Gopalan and his scientific contributions, as well as for his incredible energy. I particularly admire the width of his vision, unique in its capacity to view nutrition from an unusually broad perspective, encompassing agricultural production, anthropological issues and sociological ones along with an understanding of its economic implications.*

*I want to recall a small – but to me highly significant - personal incident. During the first session of the FAO-ICN Advisory Committee meeting in Rome, he openly defended me from the rude public attack of the FAO-appointed Chairman of the committee, who had reprimanded me for obstructing his intention to speedily marshal the entire Committee to his own pre-established conclusions. Indeed, Dr Gopalan's was the only voice that came to my rescue. It was great fun! And I still feel indebted to him for such a gallant gesture. I was truly impressed.*

*I wish him a wonderful celebration of his 90<sup>th</sup> birthday. My warmest greetings and best wishes to Dr Gopalan for the next one hundred years!*

## *Dr GOPALAN: A PHENOMENON*

*Gabr M*

*Past President I.U.N.S., Prof of. Paediatrics, Cairo University, Egypt*

*Dr. Gopalan has dedicated his life to improving the nutritional status of the most vulnerable groups in Third World countries. I first met him at a meeting on malnutrition organized by the International Union of Nutritional Sciences (I.U.N.S.) in Lausanne, Switzerland, in 1972. Several nutrition scientists from developing countries were attending the meeting. In his opening address Dr. Gopalan stressed that, although we represented the scientific "elite" of our respective countries, we would always think of the majority of people in our nations who are poor, undernourished and uneducated, and who have put their faith in us to solve their problems.*

*Dr. Gopalan is a courageous scientist who never hesitated to express and defend his point of view even in the face of great opposition. In the early Sixties, the theory of adaptation to undernutrition through stunting was widely accepted by Western scientists. In several articles he strongly argued that the "adaptation to malnutrition" approach disregards the long-term negative effects on cognitive abilities and productivity. The scientific debate continued for several years and his views were proved to be right. In the Eighties too much attention was given to child survival. Dr. Gopalan argued that efforts to support child survival should proceed in parallel with efforts to improve the quality of life for children. Thanks to his efforts this view is now adopted through the integrated management of childhood problems.*

*Dr. Gopalan has been a scientist with a vision. He argued against the etiological differentiation between marasmus and kwashiorkor. He considered both as two faces of the same coin, caused by the same multifactorial etiology. The academic community now accepts this view. His vision for the future often looked revolutionary at the time he propounded it, but time and again his visionary foresight proved to be correct. He analyzed future scenarios clarifying the dynamicity of the various factors contributing to malnutrition. Even in his own country, India, where scientists were hailing the Green Revolution, he insisted it*

*should not be at the expense of the production of pulses, which have high nutritive value.*

*Dr. Gopalan is a leader in his field, both at the national and international levels. He developed the National Institute of Nutrition at Hyderabad and inspired many of us in developing countries to follow the example. His great achievement was in laying the groundwork to ensure its sustainability and high quality research. He always encouraged young scientists to excel.*

*His presidency of the International Union of Nutritional Sciences was a milestone in the history of that organization. He managed to foster cooperation between academic institutions of the North and the South. It was Dr. Gopalan who started to identify a task or project for each I.U.N.S. Committee. Priority was given to projects with a direct impact on the health and nutrition of the community.*

*Dr. Gopalan is a phenomenon that is not easy to replicate, especially in the third world. He is not only an internationally renowned nutrition scientist but also a devoted nationalist respected by all factions in India, a fluent speaker and writer. He has excellent command of English and is able to express his views in an attractive, clear manner. His ability to defend his point of view logically on the basis of scientific evidence is remarkable. .*

## *I WISH I HAD MET HIM EARLIER*

*Ganesh K*

*Former Professor, Obstetrics and Gynaecology, Maulana Azad Medical College, New Delhi, India*

*I had heard about Dr. Gopalan and the National Institute of Nutrition since the time I was a postgraduate student. I admire his high thinking, and his ability to convey what he expects or is looking for in simple language. He is always figuring out strategies for improving the nutritional status of both the rural and urban populations, especially the poor.*

*Occasionally, he has shared his thoughts with me. He does not like too many abbreviations used by younger doctors these days, as it is difficult to absorb too many of the same used in a span of 8-15 minutes during any presentation, and I share this feeling with him.*

*I met him in the year 2001, and I wish I had met him earlier, in my younger days, when I was not too enthusiastic and no one had stimulated me to understand more about the subject. As a matter of fact, nutrition as a subject was discussed with us in a patchy way and dealt with differently by different teachers in an indifferent manner, which was boring!*

*All my fellow-students shared this feeling. Dr. Gopalan has been the only person who has been able to change my attitude towards the subject of Nutrition through his articles and personal contact. I wish him many more productive years during which I can continue to get his blessings and affection.*

## DR GOPALAN: A LEGEND

Ghosh S

Consultant, Maternal and Child Health, New Delhi, India

*What can one write about a legend who is synonymous with nutrition research not only in India or Asia but the whole world. I am a pediatrician but my deep interest in nutrition has been fired in no small measure by Dr. Gopalan.*

*My mind goes back to the first Asian Congress of Nutrition, which was held at National Institute of Nutrition in Hyderabad in 1971 under the leadership of Dr. Gopalan who as Director and with a devoted team of nutrition scientists organized this outstanding event. He was everywhere looking into every detail and meeting all the scientists from various parts of the World and delegating responsibility where it was needed. He had equal care for young scientists for whom it must have been first exposure to the galaxy of nutrition scientists from various parts of the World.*

*I had the privilege of meeting him several times when he was Director General, Indian Council of Medical Research and I was Head of the Department of Pediatrics at Safdarjung Hospital across the road. He was always accessible and supportive of any problem concerning the various research projects, which ICMR was funding in spite of his busy schedule, which he adhered to with clockwork precision.*

*During his term both at NIN and later at ICMR Headquarters, NIN went from strength to strength and contributed tremendously to furthering research in nutrition.*

*An important landmark in his remarkable career has been the setting up of Nutrition Foundation of India. I visited him several times in his one room office on the second floor of India International Center, directing and planning hundred of things that needed to be done, and at times dozing off sitting in his chair with piles of papers before him. He would debate about the plans for the building, what the logo should be etc.*

*Today NFI stands as a center for research and training on various aspects of nutrition, growth and development. And sharing views, a bi monthly*

*publication on various aspects of nutrition, with contributions from various renowned scientists, a monthly study circle meeting where various well-known persons in the field of health and nutrition as well as administrators speak followed by a lively question and answer session.*

*A two-day workshop on alternate year on different aspect of nutrition, government programmes, growth and development where distinguished speakers from various allied fields from India and abroad participate and he sits through it all!*

*Sitting in his chair in his office Dr. Gopalan oversees and directs various activities of the foundation always with a caring thought for each and every person working at NFI, and welcoming every visitor- and there are many with a cup of hot tea and welcoming smile.*

## **DR. GOPALAN: MY FATHER**

*Gopalan S*

*Executive Director, Centre for Research on Nutrition Support Systems,  
New Delhi, India*

*My earliest memory of Dr. Gopalan is of him holding me in his arms and strolling in the verandah of our house in Marredpally in Hyderabad. At that time he was the Director of the Nutrition Research Laboratory in Hyderabad – later known as the National Institute of Nutrition. The family subsequently shifted to Tarnaka within the campus of the Institute. It was in this new environment that I spent most of the early years of my childhood. The memory of the pigeons and rabbits that Dr. Gopalan kept as pets (for my amusement, I'm sure) is still very fresh in my mind, because it was I who spent a considerable amount of time with these creatures.*

*During my early childhood itself, I had heard that Dr. Gopalan was a very hard taskmaster and expected perfection of execution in any task assigned to his staff. His displeasure was displayed in the form of an extremely angry outburst in a very loud voice, clearly audible to all in the vicinity. Although he had a reputation of being a terror, I also came to know that he had acquired a reputation among his colleagues for honesty, impartiality and hard work, and he was respected for this. I found it very difficult to digest the idea that he was an extremely short-tempered person, because I always found him smiling and playful when he interacted with me! He subsequently became the Director General of the Indian Council of Medical Research and so the family shifted to New Delhi. I entered middle school and subsequently high school in this new environment, and it was during this period that I was made clearly aware of his expectations regarding academic performance – in my case this translated to marks in the final exams. I soon realized that any poor academic performance would not be tolerated, and this was conveyed to me as the years progressed.*

*Today, when I look back at those years, I realize that it was only the love and concern of Dr. Gopalan for me that motivated me and spurred me on to choose the path I have chosen for myself today. I realize that I owe a lot to him and in fact, quite literally, my very existence – he is my father!*

**THE INSTITUTION-BUILDING MENTOR I HAD THE  
PRIVILEGE TO HAVE: DR C GOPALAN**

*Jagannathan S N*

*Emeritus Professor of Pathology, West Virginia University School of  
Medicine, Morgantown WV, USA*

*We are aware that in his post-NIN/ICMR/WHO official retirement years, Dr. C. Gopalan founded the Nutrition Foundation of India (NFI) and has been guiding this Institution (as he did the NIN for many years) to function as an active proponent of nutritional health of the people of India. I am delighted that the Foundation has decided to bring out this Festschrift to honour the immense contribution of Dr. C. Gopalan to the science and practice of Nutrition over a period of six decades. I value the privilege I had of being the first graduate student of Dr. Gopalan, starting in the late Fifties at the Nutrition Research Laboratories (NRL) in my hometown of Coonoor, and moving along with him and the entire staff to our new location in Hyderabad, AP.*

*With a bachelor's degree from the University of Bombay, I joined the Haffkine Institute in Bombay and found myself in a Department of Nutrition. Browsing through scientific journals in the department, I soon realized, that the best place for me to learn how to do research in Nutritional Science, was at the NRL in Coonoor. It was no surprise that I packed up and moved back to my hometown. My father, S.R. Narayana Ayyar, took me to see Dr. Gopalan who introduced me to the then Director, Dr. V.N. Patwardhan. They suggested that I take the only position they had, "Voluntary Research Worker", as "Mr. Narayana Ayyar doesn't need your money". For my Masters degree I worked with Dr. Patwardhan on the problem of Protein and Vitamin A Metabolism. During that time, I had a feeling that I was just on the sidelines while the triumvirate of Gopalan, Venkatchalam and Srikanthia were making headlines nationally and internationally for their nutrition research. I was lucky that Dr. Gopalan offered me a position as a Research Assistant in his new research programme on Diet and Atherosclerosis and guided me for years to help me gain a Ph.D degree from the University of Bombay.*

*We were among the early group of Indian workers who undertook epidemiological surveys of Indian populations for some risk factors for*



coronary heart disease (*Ind. J. Med Res.*, 1960) Our studies were carried out in the two southern states, Tamil Nadu and Kerala, among the low-income and high-income civilian populations in and around the Coonoor area, and also among the military folks....the "other ranks" in the Madras Regimental Center and also the defence services officers in the Military Staff College in the nearby Wellington Cantonment. Also, we camped at the Trivandrum Medical College in Kerala and studied the well-to-do and the poor populations. My specific job was to analyze blood for serum cholesterol and some other constituents. I am mentioning this more to point out how meticulous Dr. Gopalan was in making sure about the accuracy of laboratory methods in research. Before letting me start on the project, Dr. Gopalan collected blood from some of us and sent the samples to the doyen of cholesterol epidemiology research then, Professor Ancel Keys in Minnesota, USA, to make sure our lab results were comparable to the standards in his lab. Incidentally, the data from our studies involving the low-income groups in the two States showed that, provided the intake of calories derived from dietary fat is low, the type of fat may not influence cholesterol levels. It was a different story with regard to the well-to-do military officers who were consuming high amounts of fat.

Dr. Gopalan then initiated me into work with experimental monkeys as well as human volunteers on various diets. In view of our results on cholesterol levels, particularly in the military officers who were consuming high amounts not only of butterfat (ghee) but also Dalda, we decided to probe the effect of the trans-fatty acid containing hydrogenated fats on serum cholesterol. Dr. Gopalan arranged with the Hindustan Lever group in Bombay to make available to us hydrogenated fat preparations containing varying amounts of trans-fatty acids. We did extensive studies using these fat preparations in macaque monkeys and human volunteers. I am mentioning these studies to point out the special mentoring I had the privilege to receive from Dr. Gopalan. I wrote drafts of two manuscripts on this work on monkeys to be sent for publication. After helping with editing the papers, Dr. Gopalan, to my great surprise, wrote only my name as author of these two papers. He explained that I had done the work and written the paper well, and that it would help me in my career to have them published under my name as the sole author. Something like this happening to a young researcher was unheard of in Indian scientific

*circles at that time. He also suggested we send the papers abroad for publication. The two single-author papers published in the Journal of Nutrition in 1960 probably helped in readily fetching me a confirmation of a postdoctoral fellowship in Canada even while I was awaiting the viva voce examination for my Ph.D thesis. I would like to add that the observations from our early studies on trans-fats initiated by Dr. Gopalan are still very much in vogue here. Recently, many cities including New York City have banned trans-fats from restaurants.*

*A few years after returning from Canada, I told Dr. Gopalan that I had applied to immigrate to the US. Dr. Gopalan did not appreciate my move. In the subsequent months, he let me see letters from a number of Indian scientists who were applying to him for research positions at NIN. Before I could be dissuaded, I received my US immigration visa within 4 months of my application; thereafter, I believe that it was because of the reputation of Dr. Gopalan and his Institution, the NIN, that I readily secured acceptance in 3 out of the 5 positions that I had applied for in the US.*

*IN 1985, I came to know that Dr. Gopalan was to give a key-note address at the International Congress of Nutrition in Brighton, UK. I attended the meeting. I recall that Dr. Gopalan's address under the category of Global Issues created much interest at the Conference. I accidentally found out, while talking to someone at the lecture recording and sale section of the Conference, that Dr. Gopalan's talk was the one most sought-after from among the lectures that day. I felt as if I myself was shining in the reflected glory of Dr. Gopalan!*

*In the formative years of my career, I had attempted to take Dr. Gopalan as my role model, particularly as regards the scientific way in which he approached any research problem, not to mention the way he organized his talks and writings on any subject. I believe my academic career here in the US benefited by this role model I had in mind, and helped me in my scientific associations with stalwarts in atherosclerosis research, especially during the well-recognized PDAY Study (Pathobiological Determinants of Atherosclerosis in Youth) that was funded by the NIH.*

*A wise man said, "An Institution is the Length and Shadow of a Single Man". I wonder whether there has ever been any other medical scientist in India who has actively pursued single-mindedly for this length of time, a health issue that is most relevant to the welfare of a large section of the Indian population.*

## **DR. GOPALAN AND THE WHO - SEARO**

**Ko Ko U**

*Emeritus Regional Director; WHO - SEARO, Yongoon, Myanmar*

*I was very pleased to learn that my dear friend Gopalan will be completing 90 years this November, and that a Festschrift is being brought out on this occasion.*

*When I was contacted in February 2008, with a request to contribute to the Festschrift, I decided that I would write about three aspects of his work in WHO's South East Asia Region. The first will be about his chairmanship of Regional ACMR, which he personally took care to develop in its early years. The second will be about his three-volume situational analysis about the future of nutrition and nutrition research in South East Asia. The third will be about his energetic and important contribution to the Goitre Control Programme in India, especially his efforts to convince Prime Minister Rajiv Gandhi of the importance of universal salt iodisation for IDD control in India. He was deeply concerned when the ban on the sale of non-iodised salt was lifted in 2002 despite his strenuous efforts. However, he was happy to witness the reimposition of the ban on the sale of non-iodised salt in 2006-07.*

*I had planned to get the relevant material from the WHO office and NFI office and prepare the article. However, with the devastating cyclone in Myanmar, there were several communication gaps and I was unable to complete and send the write-up I had planned. However, I am writing an article on his important contributions as Chairman of the first SEA/ACMR in its formative years, which will be shortly published in the History of Medical Research in WHO being brought out by WHO Head Quarters in Geneva.*

*I wish him a long and healthy life beyond his 90s and wish him all the best for further efforts and achievements in medical science particularly health and nutrition.*

**Dr. GOPALAN AND THE FEDERATION OF ASIAN  
NUTRITION SOCIETIES**

*Kim SH*

*President, Korean Food and Nutrition Foundation, Seoul, South Korea*

*I am very happy to learn that a Festschrift will be released on Dr. Gopalan's 90<sup>th</sup> birthday and that this will be followed by a two-day International Symposium on Maternal and Child Nutrition in which leading nutrition scientists from India and abroad will be participating. The fact that he is healthy and continuing to work towards improving the health and nutritional status of the vulnerable groups is the best testimony that he is an excellent nutrition scientist who practices what he teaches. He is the Father of the Federation of Asian Nutrition Societies. He inspired me with his contributions to the IUNS and the Asian Nutrition Society. I have fond memories of working with him for the IUNS Congress and the Asian Congress in Korea. I will pray for his centennial birthday and his good health.*

## DR GOPALAN: THE COLOSSUS IN NUTRITION SCIENCE

Krishnaswamy K

*Former Director, National Institute of Nutrition, Hyderabad*

*Padma Bhushan Dr. Gopalan, FRS, a nutrition scientist par excellence, is the celebrated and renowned expert behind the progress and development of nutritional sciences not only in India, but through out the world especially in South-East Asian and other developing countries. The edifice of nutrition science stands to day on the firm foundation laid by Dr. Gopalan. A great visionary with a missionary zeal, an astute intellectual with a deep understanding of the country's needs and, above all, a patriot with confidence in the country's scientists to lead nutrition science to the forefront, he has helped to sculpt the entire nutritional sciences scenario in the country. Even at the age of 90 years he is a power to reckon with and the policy makers and Government officials look up to him for suggestions and guidance. He is the unparalleled visionary, the avant-garde scientist, who nurtured nutrition science in this country right from its infancy and inspired several others to take up the profession. His thought-provoking ideas for eradication of undernutrition in Third World Nations are admired by one and all. He is the uncrowned monarch of the Indian nutritional scenario, and has carved a special niche for himself in the field. An adept administrator and institution builder, he spearheaded the cause of nutritional sciences. His dynamic leadership paved the way for food and nutrition policies and innovative strategies to combat the problems of malnutrition. His lifelong contributions have clearly brought out the fact that malnutrition is a major impediment to national development. He is a pragmatic planner and a firm decision maker with an international reputation, and is acclaimed for his frank and forthright views on the nutritional problems of developing countries and their plausible solutions. He is the champion of food-based approaches, and believes that it is the 'Farms' and not the 'Pharmacies' that can provide answers to our problems. The National Institute of Nutrition and the National Nutritional Monitoring Bureau at Hyderabad, The Food and Drug Toxicology Research Center and the National Center for Laboratory and Animal Sciences, in Hyderabad, and the Nutrition Foundation of India, Delhi, are standing testimonies to his efforts, commitment and dedication to nutrition and allied sciences.*

*Personally, I am greatly indebted to Dr Gopalan for having shaped my career and guided me through my sojourn in the field of nutrition. When I first met him I was a fresh medical graduate who knew nothing about either nutrition or research, but I was impressed by his compelling presence. His intuitive decision that I would be suitable for the organization filled me with courage and confidence. He is a person who can judge others in a matter of seconds and can motivate, persuade, enable, empower and energise the youngsters. At the same time he is a strict disciplinarian, and when he is around in the laboratories you can never see anybody in the corridors whiling away time. If you see the library full of youngsters after working hours, you know he is in town. With his innovative strategies, he made all of us work hard, read the current literature, speak at seminars/journal clubs and write research papers and submit them without typographical errors. No one would dare to apply for casual leave on seminar/journal club days. To me he is a role model of courage, competence, conviction and credibility. But for him I would not have completed my post graduation in internal medicine, given my family responsibilities. His dictionary does not contain 'I cannot do' and he hates excuses for not delivering work on time. He is truly a great leader who lifted me to higher standards, helped me build my personality, and inspired me with confidence in myself. With his strict yet empathetic nature, he made me learn, seize opportunities, leap forward, lead and achieve goals. It has been a pleasure to work under his leadership and I humbly pray to God to give him many more long years of healthy, productive and prosperous life to benefit the Nation and leave an indelible impression on posterity.*

*My humble salutations to Dr.C.Gopalan, the father of nutrition science in India.*

## **DR. GOPALAN: THE NUTRITION GIANT**

**Nandi B K**

*Senior Food and Nutrition Officer,*

*FAO Regional Office for Asia and the Pacific, Bangkok, Thailand*

*Like many others, I was fortunate and privileged to be associated with an eminent person like Dr. C. Gopalan. One feels puzzled as to where to start if one wishes to say a few words about him. I heard his name while I was a student. I first met him personally at the National Institute of Nutrition, Hyderabad. I used to maintain a close interaction with him at Nutrition Foundation of India (his second child after NIN!). At that time I was with the Food and Nutrition Board, Government of India, in New Delhi. My involvement with him and with NFI then intensified. It continued to grow further when I joined FAO. My meetings with Dr. Gopalan have been quite frequent (at least once a year) even though I am living abroad. Based on his outstanding accomplishments and the noble example he has set for all of us and for the entire community, I feel the various awards bestowed on him can be seen only as a matter of formality. The true reward for a scholarly guide like Dr. Gopalan is in the recognition and acceptance of his vision for the nutrition mission by the entire world's nutrition community. His contribution in the Advisory Group of Experts (AGE) for the FAO/WHO International Conference on Nutrition (ICN), held in Rome in 1992, was at the highest possible level at an international arena. It is an honor for me to have this opportunity to contribute my tribute to a "Nutrition Giant" of the century.*



## **GOPALAN: OUTSTANDING MEDICAL SCIENTIST**

*Padmavati S*

*President, National Heart Institute;*

*Founder Member of the Governing Body of Nutrition Foundation of  
India, New Delhi, India*

*I first met Dr Gopalan in 1947 while I was a postgraduate student in London and he a Nuffield Fellow working under Prof. Platt for his D.Sc & P.hd in London University. I have had the privilege of watching his career over this long period and it has been one unbroken series of scientific achievements in the field of Nutritional Science. Knowing the family intimately has also helped in my assessment. There is no doubt that, with his international stature, he is one of the few outstanding Indian medical scientists in the post-Independence era.*

*His qualifications, D.Sc, PhD from London University and the rarely bestowed Fellowship of Royal Society (FRS) are outstanding. The present international status of the National Institute of Nutrition is entirely due to him. The NIN Hyderabad has achieved world status thanks to his efforts and is considered the Mecca of nutrition science in Asia and indeed throughout the world. His tenure as DG, ICMR, was a golden age for the ICMR. I have personally been witness to the events during this period, when research of a very meaningful kind relating to problems special to India were conducted all over the country. As the first President of the IUNS, President of the 1<sup>st</sup> & 9<sup>th</sup> sessions of the Asian Congress of Nutrition, Member, Nutrition Expert Panel of the WHO/FAO for over 30 years, and first Chairman, Regional Advisory Council on Medical Research of the WHO, he raised Indian science to great heights by his masterful handling of the problems faced worldwide. His name is a byword in all Asian countries, Europe and the USA in the field of Nutrition. After retirement, he founded the NFI in 1980 and it has become another landmark in the world of Nutrition.*

*Dr. Gopalan's main achievements have been the promotion of nutrition science in all its aspects in post-Independence India. This includes institution building, capacity enhancement (NIN, ICMR, NFI) of all categories of workers, doctors and paramedical personnel (in India and abroad), research of a very high order especially in respect of problems*

*peculiar to India, and population outreach. The last, which involved such measures as massive dose Vitamin A administration for prevention of nutritional blindness, use of local inexpensive foods to prevent & cure malnutrition, are measures which have gone a long way in the disappearance of the florid forms of malnutrition we used to see in India some 50 years ago.*

*The fact that even after his retirement he has been so active in all these fields is testimony to his abiding interest in this area of medical science. I am glad to write these few words to mark his attaining the ripe age of 90, still mentally active in pursuing his interests. I join his colleagues, friends and staff in wishing him many more years of productive healthy life.*

## DR. GOPALAN AND WHO'S WORK ON NUTRITION

*Plianbangchang S*

*Regional Director WHO – SEARO, New Delhi, India*

*The work of Dr. C. Gopalan, the leading Indian authority on global nutrition and health, encompasses several decades and covers numerous aspects of nutrition. Dr. Gopalan's landmark studies on the epidemiology of malnutrition in children and the public health aspects of micronutrient and trace element deficiency diseases such as beri-beri, pellagra and goiter not only led to a better understanding of these by the health and nutrition professionals in India, but also enabled the policy makers and programme managers to introduce appropriate interventions.*

*In the early Sixties, studies undertaken by Dr. Gopalan and his team in South East Asia had demonstrated that when traditional Asian diets based largely on cereals and pulses were consumed in quantities that satisfied the calorific needs, the protein needs were also met. Therefore no special protein formulations were required to address the problem of malnutrition in children. Simple combinations of local cereals and pulses were found to be effective in the treatment of children with malnutrition.*

*Dr. Gopalan was a moving force behind the establishment of the National Institute of Nutrition, India's premier nutrition research and training facility in Hyderabad, in the late Fifties. The NIN-model has since been replicated and several Member States of WHO have set up their own nutrition research, training and capacity building institutions. In recognition of its impact on the nutrition situation in India and at the international forum, WHO had designated the National Institute of Nutrition as its collaborating center, and continues to maintain a close working relationship with it.*

*In earlier years, under-nutrition was largely looked upon as a social issue related to poverty rather than as a health problem. The subject of Nutrition had not received adequate recognition as a major determinant of the health status of the population, and Nutrition did not find adequate focus in the curriculum of medical colleges. Recognizing this lacuna, WHO made a significant contribution towards the promotion of awareness of the importance of nutrition in public health and, more*

*specifically, towards the training and orientation of key medical and health personnel in the field of nutrition. As part of this initiative, under Dr. Gopalan's direction, the National Institute of Nutrition introduced a certificate course followed by a Masters Degree programme in Applied Human Nutrition for physicians. In view of its importance, the programme received both financial and technical recognition and support from WHO. At the time of its inception, the Masters Degree programme was unique in its scope and content in the developing world; it provided a comprehensive and compact training in the basic principles and practices of nutritional science, nutrition research and programme management. Students in the Masters programme also benefited from the visits of international nutrition experts arranged by WHO. It is a testimony to Dr. Gopalan's farsightedness that generations of physicians who completed the Masters programme subsequently went on to hold important positions in nutrition programme management, both at national and international levels. The Certificate in Nutrition course, which was designed to address the important need for in-service training for nutrition professionals in specific areas of nutrition, was popular and has remained a much-sought-after training course among the nutritionists in India and abroad.*

*The research agenda in nutrition set by WHO has benefited from the involvement of Dr. Gopalan, who served as the Chairperson of the Health Research Committee of WHO SEAR. The deliberations of this Committee have helped promote a better focus on nutrition in public health programmes in the Region. With the support of WHO, Dr. Gopalan was able to visit several Member States of WHO SEARO in order to take stock of the nutrition situation, study the impact of developmental programmes on the nutritional status of the people, and identify essential nutrition research priorities for the future. Based on these missions, several important documents were prepared and widely disseminated to policy makers and health personnel of the countries of this Region.*

*Organizing the Asian Congress of Nutrition has been another important contribution of Dr. C. Gopalan towards the emergence of a technical identity among the nutrition science professionals in Asia and neighbouring parts of the developing world, a concept supported by WHO in its continuing efforts at capacity building among its Member States.*

*The 'Congress' has now become a regular event in the region and continues to receive strong support from WHO and other partners. Scores of nutrition and health professionals from Asia and neighbouring countries have benefited from presenting their work to their colleagues and learning from the work and experiences of their peers. This has led towards the development of a pool of nutrition professionals able to stand on their own and address the nutrition problems affecting their own communities.*

*Very early on, Dr. Gopalan, among a handful of nutrition scientists in the world, had recognized and publicized the emerging problem of chronic diseases co-existing with chronic under-nutrition in the developing world, including India. He had warned the Government of India and the Indian public about the spiraling increase in overweight and obesity among its population, arising from radical shifts in lifestyle, occupation and dietary patterns, and leading on to non-communicable diseases such as diabetes, hypertension and cardiovascular disorders. These changes, as was pointed out by Dr. Gopalan and a few others, were also taking place amidst sizable pockets of hunger, maternal and child under-nutrition and food insecurity, giving rise to a situation that has come to be described as "the dual burden of malnutrition". In many ways, Dr. Gopalan's thoughts and writings have been in line with views that were later articulated in WHO's approach towards the control and prevention of non-communicable diseases, its global strategy on diet, physical activity and health, and its work in promoting optimal foetal development among the populations of the developing countries.*

*The creation of the Nutrition Foundation of India (NFI), a non-profit think-tank on nutrition and its impact on the health and development of the population has been another major achievement of Dr. Gopalan. NFI has coordinated operational research and nutrition policy research in promoting the health and nutrition status of the populations of India and neighbouring countries. Senior policy- and decision-makers in India and in the region consult the publications of NFI under the technical guidance of Dr Gopalan regularly. WHO, along with its other partners, has supported the work of NFI in several ways and values this collaboration.*

*WHO has recognized the importance of focusing on school children as a key entry point to improve the nutrition of the population and in modifying the health and nutrition behavior of the future generations towards a healthy lifestyle. The “nutrition-friendly schools” initiative has been launched taking these factors into consideration. Dr. Gopalan’s position that improvement of the school system and the institution of a comprehensive school health service will address the practical health needs of children and their parents is aligned with the approaches of WHO.*

*As the senior-most authority on nutrition in India, Dr. C Gopalan has had a ringside view of the evolving nutrition scenarios in India and its neighbouring countries. His encyclopedic knowledge of nutrition and wisdom has influenced, and continues to influence, the manner in which we understand nutrition and undertake design interventions to improve the status quo. Even as he approaches the tenth decade of his life, Dr. Gopalan’s pace and magnitude of work have remained undiminished and widely appreciated. WHO, and I personally, join others in wishing Dr. Gopalan many more years of work and look forward to a continuing collaboration.*

## **DR. GOPALAN: THE DOYEN OF NUTRITION SCIENCE**

**Prakash V**

*Director Central Food Technological Research Institute,  
Mysore, India*

*It is a great honour and a pleasure to write a few words about Dr. Gopalan, FRS, for the Festschrift, which is being compiled by Nutrition Foundation of India.*

*Dr. Gopalan, the doyen of the science of Nutrition in India, has been helping to steer the nutrition agenda of the country right from day one of his career. He continues to do so with the same enthusiasm and vigour even today. He has carried out studies that have addressed several nutrition problems in India and suggested approaches towards combating them; many of these studies have culminated in current national nutrition policies and programmes and in drawing up an agenda for improving the nutritional status of future generations, with a clear focus on reaching out to the needy.*

*When I first met Dr. Gopalan nearly 30 years ago at a symposium, my reaction was “how can he remember so many micro details and translate them into a macro- vision?” Even today, when he is President of the Nutrition Foundation of India, I am baffled by the same question. It is amazing how he sees the entire forest and, at the same time, has the in-depth analytical mind needed to keep track of the details of each leaf in each tree! His role in Nutrition science has not been limited to India, but has had a far-reaching global impact. Perhaps the best way for me to summarize Dr. Gopalan’s contribution is, “He is one of the greatest living legendary figures in the field of Nutrition on the globe, and indeed a great human being too. It is this combination that can make a difference for a scientist as he has been proving all his life”.*

## DR GOPALAN AND NUTRITION

Rao B S N

*Former Director, National Institute of Nutrition, Hyderabad, India*

*I have known Dr. Gopalan since 1951, when he was Deputy Director of NRL, Coonoor. He has largely promoted my research career to work on nutrition problems of India. Similarly he has promoted research career of several others.*

*He himself has made contributions in the areas of Clinical, Experimental and Community Nutrition relating to Protein Energy Malnutrition (PEM), Vitamin A deficiency of children, iron deficiency anaemia, the major problems of India. He has promoted the concept that child malnutrition is not solely due to protein deficiency, but primarily due to energy deficiency (food deficiency). This concept is now accepted all over the world.*

*He has also demonstrated through clinical and field trials practical approaches to prevent PEM, nutritional blindness in children due to vitamin A deficiency, anaemia among women (pregnant) and children. These three community trials have been adopted by Govt. to control these three deficiencies.*

*He has been committed to research entirely related to nutrition problems of the country, as the Director of NIN with devoted team of research workers, promoted nutrition research as the DG of ICMR. He has continued supporting nutrition after retirement, as the Chairman of NFI. May we continue to have his support and guidance in nutrition for which may be blessed with some more years of good health.*



## DR. GOPALAN: MY TEACHER AND MENTOR

Reddy V

*Former Director, National Institute of Nutrition, Hyderabad, India*

*My association with Dr. Gopalan goes back to 1960, when I joined NIN and he became the Director of the institute. I met him for the first time in Niloufer Hospital for Women and Children where a Nutrition Unit was set up for clinical research. I just finished my post-graduation in Pediatrics and was thinking of clinical practice, but I changed my mind after meeting Dr. Gopalan. He had that undescrivable charisma of an accomplished scientist that attracted me to nutrition research. I had the good fortune of working with a great leader with scientific vision, ideas, initiative and drive that could inspire many students like me. I started my career with research projects on protein energy malnutrition and vitamin A deficiency, the two major public health problems among children at that time. Dr. Gopalan was my mentor and teacher; he provided excellent training upon which I built my research career. Under his able leadership, the Nutrition Research Laboratory blossomed into the National Institute of Nutrition. I grew up with the Institute and followed his footsteps to become its Director in 1987. I am grateful to Dr. Gopalan, for his guidance and encouragement, which enabled me to contribute whatever I could towards the growth and development of the institute. My association with him continued even after he moved to Delhi. After his retirement he established Nutrition Foundation of India, 28 years ago and he is still guiding all its activities. His amazing capabilities and skills seem to grow with age. Some of his recent articles in the NFI Bulletin draw attention to the emerging problem of overnutrition leading to obesity and chronic diseases. I submit with great pleasure my contribution to the Festschrift dedicated to Dr. Gopalan on the occasion of his 90<sup>th</sup> birthday. I take this opportunity to pay my humble tribute and wish him many more years of healthy and productive life.*

## TO SIR, WITH LOVE

### Research Scholars

Nutrition Foundation of India, New Delhi, India

*The feeling of inadequacy disturbingly crept in when the formidable Herculean task of penning down a tribute for Dr. C. Gopalan was to be performed. Oh Lord, when has a diya shown light to the sun. The abilities were questioned by the inner self and the mind raised qualms of incompetence. But the inner struggle just dissolved itself when we reflected on our luck. This one chance of a lifetime was being bestowed on us to express our reverence, our affection, our love, our admiration and most importantly our gratitude towards Sir. After all, we have earned this by being fortunate enough to be working closely with Sir at the Nutrition Foundation of India for a few years.*

*When we were college students before we joined the Foundation, we knew Sir as “The Dr. Gopalan”, the author of our bible then. So, we were bound to be in awe of him. But then things changed with time. Now, we revere him. And this deference is not only owing to his innumerable publications of great-unmatched academic credit but it is more so owing to working and learning from Sir at a personal day-to-day level.*

*So, here we share some of our “Wonderful” reminisces...*

*We always wondered how Sir could be as enthusiastic about work at the end of the day as he was at the start. Just before leaving office, when we itched to postpone the work for the next day, Sir would make sure he briefly goes through the task then, to be able to ponder over it during the night, and would be eager to get it finished first thing in the morning. Such unmatched enthusiasm....*

*We always wondered how Sir could, every single working day without fail, reach office at 9:30 am sharp, and how it happened that traffic never came in his way! We were, of course, with no mincing of words, rightfully reprimanded for not practicing punctuality at the beginning of our professional lives.*

*We always wondered how a person who is so scientific in his thoughts, mindset and temper, could be such a graceful, flawless and impeccable writer.*

*We always wondered how a person could have such farsightedness, even in a situation of crisis. We tried some reasoning and attributed it to his experience, his expertise in his field and his prior exposure to similar situations, but none of these explained it completely. So we gave up any logical reasoning and decided "Sir just knows".*

*We always wondered how Sir could, at the successful culmination of a Workshop / Symposium, begin his vote of thanks by outlining the programme of the next workshop. This can be attributed only to his tirelessness, and his boundless and limitless energy stores.*

*We always wondered how Sir could achieve and complete so much work in a single day, when we, who had the computer for our assistance, could not even do half as much. And at the day's end, it was Sir who looked so fresh and his workstation so neat as compared to our disheveled and messed up faces and tables.*

*We always wondered how Sir could, immediately after a fun-filled cake-cutting celebration make us acknowledge the need for working harder in life and, in the next breath, ask us to sing a song and enjoy ourselves. This certainly taught us the valuable lesson that a balance needs to be maintained in every aspect of life.*

*Having read all this, the reader may have been led to believe that working with Dr. Gopalan was an easy teaching-learning experience. But, it wasn't always so.*

*Many a time, we wondered whether we would ever be able to come up to his expectations and gain his approval, though deep down we really hoped to do so. His appreciation was always a measured one, maybe out of the fear of leading to complacency among his staff, but always enough to encourage and inspire us to strive to do better.*

*So, after wondering and wondering about many things, we just learnt the reason we knew him as “The Dr. Gopalan”. He has not only been the Father, the Leader of Nutrition, but he is also a born leader, a leader who leads by example.....*

## **DR. GOPALAN: THE INSTITUTION BUILDER**

**Sabharwal M M**

*Member, Governing Body, Nutrition Foundation of India;*

*President Helpage India,*

*New Delhi, India*

*It was in the sixties when I was introduced to Dr. C. Gopalan in Calcutta by my late wife Kamala Puri Sabharwal. Dr. Gopalan had come to Calcutta to preside over a function organized by the Dietetics Society of India where my wife was deeply involved. Dr. Gopalan is one of the few gifted persons who have outstanding personality and charm, clear expression and thorough all round knowledge and draws people with ease. With untiring work and outstanding contribution in the field of nutrition over seventy years and in setting up and nurturing the Nutrition Foundation of India, Dr. Gopalan has earned a name, which will go down in history.*

*Dr. Gopalan is recognized as the father of nutrition not only in India but globally. Even to day in any major conference any where in the world Dr. Gopalan's name invariably figures during discussion of major nutrition problems.*

*Dr. Gopalan started his research career in Nutrition Research Laboratory at Coonoor, in Tamil Nadu. Within a few years, it shifted to Hyderabad – where under Dr Gopalan's stewardship it grew to become the National Institute of Nutrition (NIN). Under Dr Gopalan's leadership NIN became not only the center for nutrition research in India and for the entire South East Asian countries but also became the base for research in various nutrition related areas like food safety and, nutrition monitoring and surveillance.*

*After his retirement as Director General of Indian Council of Medical Research, he built up Nutrition Foundation in New Delhi as an institution for nutrition research with focus on nutrition policy research*

*I am personally very indebted to Dr. Gopalan for having delivered the first of the Annual Memorial Lectures at Lady Irwin College in memory of my late wife Kamala Puri Sabharwal who was an alumnus of that*

*college and nutritionist of great promise. Dr. Gopalan has presided over the Memorial Function for nearly 35 years since its inception in 1974. I wish him a long and healthy life and look forward to his continued great contributions to improvement of nutritional status of Indians.*

## **'NUTRITION' GOPALAN**

**Seshadri M**

*Founder Member, Governing Body, Nutrition Foundation of India,  
Chennai, India*

*I can't recall when I first came to hear that my father was a nutrition scientist. Certainly it must have been long before I was able to appreciate the meanings of the words 'nutrition' and 'scientist'.*

*But I do recall my grandparents (his parents) relating their conversations with friends and acquaintances on the topic of my father. The friends would ask, "We hear Gopalan is doing something called 'nutrition' up in the hills?" And they would reply, yes he is doing nutrition research in Coonoor. "But why?" they would ask, genuinely puzzled. My grandparents' standard reply, "Because he wanted to," never seemed to satisfy these friends. They could not imagine a brilliant doctor wanting to do nutrition research. Even more puzzling to them must have been why his parents had allowed him to follow his dream.*

*But this was never a puzzle to my father, who had received steady support from his parents about his career choice. They had never tried to talk him out of following his heart and choosing nutrition research rather than medical practice. And they were always proud of his achievements and the recognition he soon began to receive.*

*In school in Coonoor, my friends would often ask, "What does your father do?" "Nutrition research," I would reply. The next question often was "Does he tell people what they should eat?" And I would try to explain, as best I could at the time, that nutrition research had more to it than mere diet counseling. But they couldn't really get a handle on it. Most of them couldn't figure out why anyone would have to do research to find out what's healthy to eat. One friend told me, "My mother already knows all about healthy foods." Another friend asked me, "If he is not treating sick people, how can he be a 'doctor'?" Then I explained that he had an MD in medicine as well as a Ph.D. in Nutrition, and that he had decided not to practice medicine. "Oh," said my friend wisely, "if you don't practice hard for something you cannot be good at it. So he didn't practice enough?" I gave up at that point, I think!*

*My brother, who went to a different school, had pretty much equivalent experience, but was probably more patient with his explanations.*

*Another question my schoolfriends in Coonoor would ask, often leading to quite hilarious situations, was “Where does your father work?” My answer would be “At Nutrition Research Laboratories inside the Pasteur Institute campus.” “There’s a laboratory in the compound? Is it a new building?” “No, it’s a very old building. It used to be a jam factory.” Then, by some strange leap of reasoning, the friend would be likely to remark, “Oh, jam! Your father makes nutritious jam?”*

*Talking of jam, the trickiest part of being ‘Nutrition’ Gopalan’s daughter has been the close scrutiny I received at various stages regarding my dietary preferences. “What?” people might remark, only half jokingly, ‘Nutrition’ Gopalan’s daughter loading up on potato chips?” As for my father himself, I must say with much appreciation that the word ‘nutrition’ never played spoilsport in the goodies we put away as children (as long as we finished the vegetables first!).*

*By the time I entered high school we were in Hyderabad. A new set of friends, a new round of questions. “What does your father do?” This time the reaction was not incomprehension (obviously these were older children) but bewilderment just the same. They hadn’t heard of such a career choice. Their idea of scientific research was physics and chemistry, maybe a bit of biology. But nutrition? “Does he have to examine food stuff under the microscope?” asked one girl, with a genuine keenness to know more about this esoteric new science!*

*When it was time for me to go to college, friends and relatives of my parents were seized with a very natural curiosity about the subjects I intended to study. “Physics, chemistry and mathematics,” I told them. “What? Not medical college?” some of them would remark, (My brother was already in medical college). Others, operating from the assumption that such a rigorous course, as MBBS was not for a girl, would helpfully suggest, “Even without medical college it’s possible to enter the nutrition field.” My father’s success in his chosen profession of nutrition research and the fact that he had made a name for himself in that field, had made*



*it, in the eyes of many, a desirable career option for his daughter too, even without a medical degree to back it up!*

*While I was in Nizam College, my father was invited to deliver a lecture in the assembly hall to an audience consisting of the entire college, students as well as faculty. I was a proud member of the audience that day. My father made an inspirational speech, commending the spirit of scientific enquiry and urging the development of a scientific temper. He interspersed his speech with anecdotes and little stories, but even these were not overtly nutrition-based. When it was over and we were dispersing, one boy came up and told me, "It was a good speech, but he didn't say anything about nutrition. Everyone was saying 'Nutrition' Gopalan is going to talk to us today. But why didn't he talk about nutrition?" I had no reasonable reply I could give him, except maybe that my father had preferred to keep things general for a general audience. But I didn't venture giving him this reply, because it would have been too weak in the face of the irrefutable logic: "'Nutrition' Gopalan is expected to give talks on nutrition."*

*Then there are the things 'Nutrition' Gopalan's daughter is supposed to do. My husband and I were greeting guests at our wedding reception and acknowledging the blessings and good wishes. Things had arrived at the stage when the feet of the bridal couple get painful and the smiles get rather forced and fixed. Just then, one of my father's friends breezed up and clapped my husband on the shoulder. "Congratulations!" he boomed. "Now you will be nutritiously cared for." That quip cheered us both up, and my husband would bring it up over the course of many years, especially when we were at the dinner table. And yes, this friend gave us a gift. It was a recipe book, and I still have it.*

*Over the years, of course, my father has given enough speeches on nutrition even to satisfy those who, like my Nizam College friend, believe that when a nutrition scientist stands up to speak, he should speak only nutrition. My father has been reading, writing, speaking...even breathing nutrition. He has received the Padma Shri, the FRS, the Padma Bhushan, and a huge number of other awards. Sometimes news reports mention him as Colathur Gopalan. "Who is this?" some will ask. But there are always people who have the answer. "It's 'Nutrition' Gopalan".*

*Yes, after more than sixty five years in a career that he chose and never regretted choosing, after hundreds of research papers and speeches and a long, long, list of awards, honorary degrees and other recognitions, 'Nutrition' Gopalan, my father, is ninety years of age. And he is still reading, writing, speaking...and breathing Nutrition.*

**DR. GOPALAN: GREAT INSPIRATION TO NUTRITION  
SCIENTISTS**

*Seshadri S*

*Former Professor, Foods and Nutrition, M S University of Baroda,  
Baroda, India*

*It is indeed an honour to be invited to contribute to this volume to felicitate Dr Gopalan on his 90<sup>th</sup> birth day, for his long, dedicated and indispensable contribution to nutritional sciences and for being a guiding beacon of light and a source of great inspiration to nutrition scientists like me. Unlike many other contributors to this volume, I came into the nutrition field rather late. I was introduced to Dr. Gopalan in 1980 by Dr. Tara Gopaldas, who was at that time the Head of the Department of Food and Nutrition at M S University, Baroda. I had been teaching at that university for some time and had just begun to take a serious interest in nutrition research. It was Dr. Gopalan's spontaneous and warmly encouraging words about a presentation I made at the Dietetics Conference in 1980, where he was the Chief Guest, that provided the incentive for me to engage in the quest for solutions to some of the pressing nutritional problems in India. From then on it has been an immensely fruitful association that has contributed very significantly to my own professional growth and development. His deep insights into the changing nutrition scene in India, and the commitment and dedication he has inculcated into nutritionists like me with his highly disciplined and perceptive approach to the myriad problems in the field of nutrition, have exerted a profound influence on my own thinking and practical approach. Dr. Gopalan is not given to complimenting people easily, but when he does you know you have truly deserved it. I have fond memories of those precious occasions. I feel truly privileged to contribute to this volume, which is dedicated to Dr Gopalan.*

**DR. GOPALAN AND NATIONAL INSTITUTE OF  
NUTRITION**

**Sesikeran B**

*Director, National Institute of Nutrition, Hyderabad, India*

*I learnt in retrospect, several years after I had joined the NIN, that Dr. Gopalan had been a young medical student in the neighborhood in which my grandfather lived and had in fact helped my dad and his brother through their illnesses as a young MBBS physician (they were a rare breed in the late 1930's and early 40's) neighbour. When I was preparing for my interview for the post of Assistant Research Officer at National Institute of Nutrition (NIN) I had read about many of the contributions of Dr. Gopalan; I realized he was almost synonymous with the NIN. It is perhaps providence rather than coincidence that NIN and Dr. Gopalan were born in the same year.*

*By the time I joined NIN, Dr. Gopalan had become the Director General of the Indian Council of Medical Research. During one of his visits to NIN; he wanted to meet all the new young recruits. We all assembled in the Director's office one afternoon in the presence of the Director, Dr. S. G. Srikanthia. We were awe-struck to see in flesh and blood the person about whom we had heard and read so much. In a couple of minutes he unrolled before us his vast expertise in the area of nutrition research, and told us how meaningful nutrition research would be for us and for society. I consider it my good fortune that I am today heading the institution that Dr. Gopalan did so much to build and put on the international nutrition research map when he was its Director. I would have done my bit if I can achieve even half of the immense contribution he has made to NIN. Even to this day "Dr. Gopalan's days" are considered as a benchmark, which, as the current Director I know is difficult to achieve.*

*He was commanding and yet considerate, knowledgeable but yet willing to learn from anyone who had some new information. His presence in the Annual Conference of the Nutrition Society of India adds value to meetings and attracts significantly greater participation. Even to this day his clarity of thought and commitment to nutrition research is remarkable. His very presence is inspiring to us and we wish he will continue to inspire us for many more years to come.*

## DR. GOPALAN AND LADY IRWIN COLLEGE

*Siddhu A*

*Director, Lady Irwin College, New Delhi, India*

*Dr. C. Gopalan is very special to Lady Irwin College. All the students have benefited from the wealth of knowledge he created in nutrition with his highly focused and dedicated work. His articles and writings have been the gospel for training most of the contemporary nutrition practitioners. He has continued to write about his concerns in the NFI Bulletin, and these articles have given direction to serious researchers. He has built several institutions and professional bodies and has always extended his support to the students of Lady Irwin College. The students are privileged to visit NIN, Hyderabad and attend NSI meets. The Nutrition Foundation of India, set up in New Delhi, gave a further impetus to quality thought processes in Nutrition. The NFI study circle meetings throw up brainteasers for students, and provide a forum for meeting pioneering workers in nutrition. Dr. Gopalan has been a selection committee expert, examiner, and governing body member at our college. He also delivered the first Kamala Puri Sabharwal Lecture. He gracefully chaired these lectures in subsequent years and made valuable presidential remarks after most of them. We are deeply indebted to him for his contributions to our college and more so to the field of Nutrition. He is a true mentor to the Department of Food and Nutrition of the college. Dr. Gopalan is easy to admire but difficult to emulate. With all humility I congratulate him for his remarkable achievements, and deeply acknowledge his contribution towards producing competent nutritionists for this country.*

## **DR. GOPALAN: THE GREAT NUTRITIONIST**

**Tontisirin K**

*Professor Emeritus Nutrition, Institute of Nutrition Mahidol University, Salaya, Thailand and Former Director, Nutrition and Consumer Protection Division, FAO HQ, Rome*

*Dr Gopalan is a name known to the world as a nutrition champion of the century. He took initiative and great effort to make nutrition science as a major contribution to medical sciences and public health when India was struggling hard to address the nutritional deficiencies such as protein-energy malnutrition, beri-beri, pellagra, etc. in the country. Nutrition in medical sciences during those days was not considered something lucrative as a career. Dr. Gopalan took the challenge to demonstrate the world that how a challenge can be converted into opportunities which many of us even today cannot find the transformation an easy task. At that time he started his journey with the Nutrition Research Laboratory in Coonor, which was then turned into the National Institute of Nutrition (NIN) in Hyderabad. Dr. Gopalan with his incredible urge for research moved from Hyderabad as Director, NIN to Delhi as the Director-General of the Indian Council of Medical Research (ICMR). He led the nutrition research to a high, which was recognized as the golden era of nutrition sciences in India. His contribution during that phase was seen to be most rewarding since he could put the nutrition agenda in the limelight. Upon retirement from the ICMR he started his own organization, the Nutrition Foundation of India (NFI) which has now become an institute of repute in its own rights. His scientific work has made him a person of eminence in the area of nutritional sciences. The world nutrition community has seen him in many honourable positions such as President of the International Union of Nutritional Science (IUNS) and also the Asian Congress of Nutrition (ACN) first held in India under his initiative besides a member of the Advisory Group of Experts (AGE) for the International Conference on Nutrition (ICN) held in Rome in 1992. He was a recipient of many distinguished awards at national and international levels. He is a person with high integrity, leadership, eager to learn and a great deal of sympathy to help the poor and disadvantages. It will not be an exaggeration to say that the word "nutrition" and "Gopalan" are synonymous not only in India and Asia but also in the*

*entire world. We feel honoured to pay our tribute to this great man of nutrition world of the present time.*

## **DR. GOPALAN: A SPECIAL AND UNIQUE LEADER**

**Vijayasarathy C**

*Former Faculty of NIN; Currently Staff Scientist, National Eye  
Institute,  
Bethesda, USA*

*I am writing this to express my deep admiration and respect for the leadership that Dr Gopalan had displayed while serving as the Director of the National Institute of Nutrition, Hyderabad, India. Dr. Gopalan's days at NIN meant a lot to me in terms of inspiration, motivation and recognition. His leadership motivated me to aspire to higher goals unthinkable for a guy like me who started as a Laboratory Assistant. The kind of environment that he and his colleagues, in particular Dr B S Narasingha Rao , Dr. P G Tulpule and Dr M S Bamji, nurtured at the National Institute of Nutrition, enabled me to acquire new skills and knowledge and facilitated my transition from a laboratory assistant to a scientist. My move from NIN, Hyderabad, to National Institutes of Health, Bethesda, USA, was a tough one, but exciting and rewarding in terms of science, travel opportunities and friends.*

*Rarely does the Director of an Institute entrust important tasks to a fresh laboratory assistant. When I was introduced to Dr. Gopalan (along with Kumar, another fresh entrant) by Dr. Bamji, his advice was 'show us what you are capable of and we will certainly do something for you' the words that stuck in my mind forever. When NIN acquired the automatic amino acid analyzer, the first of its kind in India, I worked closely with Dr. Narasingha Rao, Mr Surendra Prasad and a Beckman scientist to set it up. Soon afterwards I was put in charge of its operation and data analysis. Then, one Saturday afternoon, Dr Gopalan interrupted my work and asked me to project the slides in the auditorium for a presentation. From then on it became one of my duties. When Professor McCance complimented me for projecting the slides without making a single mistake during the Golden Jubilee celebrations, Dr. Gopalan immediately wrote a congratulatory note to me. To be frank I did not like that job and I did it because Dr Gopalan did not expect anything that was less than perfection.*



*On one occasion I was projecting the slides for a lecture that was arranged for visiting medical students. It hurt me most when I noticed that in that group there were a couple of my former class mates who were fortunate enough to have qualified as doctors by paying donations to enter medical college. I had always wanted to pursue a PhD but it remained as an unfulfilled ambition because of financial constraints and family responsibilities. Then I was reminded of Shakespeare's quote: "Sweet are the uses of adversity". I used those projection sessions as my learning lessons in biochemistry and nutrition. Those were the days when vitamins were being rediscovered as hormones and advances in molecular biology started hitting the headlines in the form of Nobel Prizes.*

*It was not even three years after I had joined NIN when, one morning, Dr Gopalan called me to his office and asked me to undergo a one-year Post Graduate Course in Radiological Physics at Baba Atomic Research Centre (BARC), Bombay. The word 'physics' scared me but at the same time the thought of going to Bombay excited me. Since I had not completed even 3 years of service, I was not eligible to apply for study leave. Dr Gopalan asked me to resign from my job with the assurance that I would be reappointed soon after completing the course at Bombay. At that time I was not aware that he was preparing me for the IAEA project on salt fortification with iron, a work that involved extensive synthesis of radioactive Fe-55 and Fe-59 labeled iron compounds.*

*The experience at BARC was overwhelming and the scientific environment there further ignited my desire to achieve something worthwhile. Mathematics and Physics were tough but Particle Physics fascinated me. Samuel Glasstone's 'Source book of Atomic Energy' made things easy for me to understand. During my college years, I read of Bhabha's predictions about the existence of the 'meson' a sub-atomic particle, but what was unknown to me was that Bhabha was an artist and painter. Apart from the quality science that was being carried out at BARC, in that wide, sprawling campus I also sensed beauty and perfection everywhere. It soon dawned on me that both Dr. Gopalan and Bhabha were perfectionists and both shared the same vision and zeal to place India on the world map in their respective fields.*

*Upon successful completion of the course I returned to Hyderabad and Dr. Gopalan re-appointed me as Technical Assistant. What followed were the most productive years of my life in terms of science. I am greatly indebted for this not only to Dr. Gopalan but also to Dr Narasingha Rao. With Dr. Rao the relationship was one of mutual confidence rather than authority. Doing science with him was not only challenging but also a thing of joy. I got involved in many research projects and in programmes that trained high profile visitors on the use and application of radioisotopes in medical research. The research projects included: iron absorption from Indian diets as assessed by Whole Body Counter, feasibility of salt fortification with iron and iron absorption from iron fortified salt; chromium absorption studies; and calcium turnover studies in patients with fluorosis and endemic genu valgum. For my efforts, I was credited as a co-author in all the publications that resulted from those studies, something unique for a member of the technical staff in a scientific institution.*

*The more I enjoyed science, the more restless and insecure I felt. My mind never drifted away from the thoughts of pursuing a graduate course in biochemistry. I became bolder and even considered leaving my secure job so that I could fulfill my desire. Things got stabilized at the home front with the support of my younger brothers. I started applying, and finally got admission at the prestigious Post-Graduate Institute of Medical Education and Research (PGI) at Chandigarh. When this news reached Dr. Gopalan and Dr. Narasingha Rao, Dr Gopalan came up with the suggestion that I should seek admission in the local Osmania University and then continue my research in the evenings, a great idea indeed. Dr. Gopalan promised to talk to the University authorities and make this a possibility. Based on this I cancelled my trip to Chandigarh. The University took its own time, and by the time I came to know about their unfavourable decision, it was too late for me to get into PGI. When he heard the news Dr. Gopalan was distraught and I sensed that he felt my pain and disappointment. He left the scene with the comforting words "something should be done." That was when he created the posts of Technical Officers, a position on par with Assistant Research Officers. Soon I was promoted to that position along with Mr. Jacob. These positions, created for the first time at NIN, offered better pay and career*

*prospects for the technical staff. In short he created a legacy for the technical staff at NIN.*

*When Dr. Gopalan moved to the ICMR headquarters at New Delhi as the Director-General, the entire staff of the Institute came to Begumpet Airport to see him off. In 1977 I completed 10 years of service at NIN and applied for a 2-year study leave to go to Chandigarh and pursue a PG course in biochemistry. It was initially met with stiff opposition from the administration, but finally I had my way. In short, I completed the course in 1979 and thanks to Dr Tulpule, I was permitted to register as a PhD candidate with Dr.Narasingha Rao as my supervisor.*

*I came to the USA in 1987 to pursue post-doctoral studies at the University of Pennsylvania, Philadelphia. In 2001 I moved to the Faculty of Medicine, United Arab Emirates University, United Arab Emirates, to teach Biochemistry and Molecular Biology to medical students. In 2004 I returned to the USA and joined the National Eye Institute as a Biochemist (Staff Scientist). I am currently working on the molecular mechanisms that underlie macular degeneration, with particular reference to X-linked retinoschisis in young males. Our group is targeting gene therapy as an approach to treat this disease. My work at the University of Pennsylvania focused on the biogenesis of mitochondria and the interaction between the mitochondrial and nuclear genomes.*

*People say that I worked hard but I do not feel that way. There are so many people in the work environment who also work sincerely and put in their best efforts. Most often, their efforts are not recognized or go unnoticed. Dr. Gopalan could change my life because of his leadership style and his direct interactions with me. He exemplified dynamic leadership that recognized talent, motivation and hard work.*

*When we look back into history we always cherish the memories of certain individuals or certain time frames with special tags: like Camelot associated with Kennedy, or the golden age of the Gupta Empire. For me Gopalan's days at NIN were of that special and unique nature. He brought the world to the doorsteps of NIN. The days were full of vigour and enthusiasm. There was science in the air and if those walls could talk, they would have whispered science.*

*Dr. Gopalan always set an example and when it was time for him to leave the stage he left with grace and dignity. Even now he continues to pursue his passion with the utmost dedication. May God bless him with many more years of happy, healthy and productive life.*

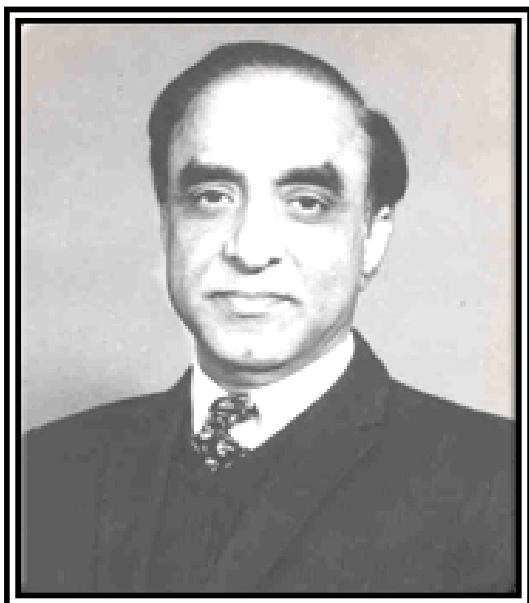
**DR. GOPALAN: COMBINING SCIENCE WITH POLICY**

*Willetts WC*

*Chair, Department of Nutrition, Harvard School of Public Health*

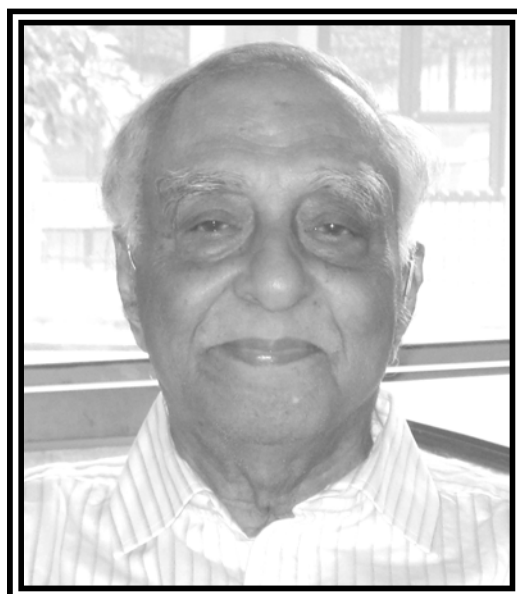
*Boston, MA, USA*

*I regret not being able to join in person for this event in honour of Dr Gopalan. Nevertheless, I do want to convey my admiration for all he had done to promote good nutrition and well being for so many people, not just in India but around the world. He has provided a stellar example of how to combine science with policy to benefit mankind. We have much still to do, but he has created a good path. With best wishes on this special occasion*



**Section – 3**

**SIXTY YEARS OF DISTINGUISHED LEADERSHIP  
IN NUTRITION**



# SIXTY YEARS OF DISTINGUISHED LEADERSHIP IN NUTRITION

## Academic Qualifications

- F.R.S., MD (Madras). Ph.D. (London), D.Sc. (London), D.Sc. (Hon. Caus. Banaras Hindu University), F.R.C.P. (Edin.), F.R.C.P. (London)
- Fellow of the Royal Society, London, F.R.S.
- Fellow of the Indian National Science Academy.
- Fellow of the Indian Academy of Science.
- Fellow of the National Academy of Medical Sciences of India.

## Current Position

- President, Nutrition Foundation Of India, New Delhi-110016

## Previous Positions

- Director-General Indian Council of Medical Research, New Delhi, 1974-79.
- Director- National Institute of Nutrition, Hyderabad, 1960-1974.

## Other Positions Held

- President, International Union of Nutritional Sciences, 1975-79.
- Chairman, Regional Advisory Committee on Medical Research, WHO, 1975-1980.
- Member, Global Advisory Committee on Medical Research, WHO, 1977-80.
- Member, Nutrition Expert Panel of the WHO/FAO for several years and participated in all the major meetings of the panel during the last 30 years.
- Founder President, Nutrition Society of India.
- President, First Asian Congress of Nutrition.
- Elected Honorary Member of the American Institute of Nutrition.
- Elected President of the Ninth Asian Congress of Nutrition

## Academic Honours

### *Awards and Prizes*

- Basant Devi Amir Chand Prize of the Indian Council of Medical Research in 1954 for medical research.
- Basant Devi Amir Chand Prize (Senior) of the Indian Council of Medical Research for 1960 for research in nutrition and public health problems.
- Amrut Mody Research Award for 1972 for contributions in the field of nutrition.
- Dr. B.C. Roy National Award for "Development of Specialities in Medicine-Nutrition" (1974).
- Ambuj Nath Bose Prize of the Royal college of Physicians, London, 1976.

- Dhanvantri Award for outstanding contribution in Medical Research and Leadership in the field of nutrition and medical research, 1978.
- Federation of Indian Chambers of Commerce and Industry Award for contribution in the field of nutrition, 1978.
- WHO-Health for All Medal, 1988.
- Sir C.V Raman Gold Medal of the Indian National Science Academy in recognition of outstanding scientific merit, 1988.
- International Union of Nutrition Sciences Award for outstanding work on nutritional problems of developing countries, 1989.
- R.D Birla Award for outstanding medical research, 1990.
- Awarded the Centenary Honorary Fellowship of The London School of Hygiene and Tropical Medicine on the occasion of the Centenary Celebrations, 1999.

### Lectureships and Orations

Has delivered numerous Memorial lectures and several Keynote addresses on Nutrition and Dietetics at Seminars, Conferences and Workshops.



**SELECTED PUBLICATIONS OF DR. C. GOPALAN  
(1944 – 1980)**

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20. C.Gopalan, S.G.Srikantia and P.S.Venkatachalam. Electrocardiograph changes in severe malnutrition, *Indian J.Med. Res.*, 43:15-21,1955.
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7	Nutritional consequences of developmental programmes	Jan, 1982
8	Reviews and comments: Nutrition in the health system	Jan, 1982
9	Nutrition in the new twenty point programme	Apr, 1982
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107	Current National Nutrition Scene: Areas of Concern	Oct, 2008

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