PROCEEDINGS

6th ASIAN CONGRESS OF NUTRITION

16-19 September 1991
Kuala Lumpur

NUTRITIONAL CHALLENGES
& FRONTIERS
TOWARDS YEAR 2000

Organised by
NUTRITION SOCIETY OF MALAYSIA

Under the Auspices of
FEDERATION OF ASIAN NUTRITION SOCIETIES

(Part 1 of 3)

PROCEEDINGS
OF THE
SIXTH ASIAN CONGRESS OF NUTRITION

16-19 SEPTEMBER 1991

KUALA LUMPUR, MALAYSIA

ISBN 983-808-012-8

Published by:

The Nutrition Society of Malaysia,
c/o Division of Human Nutrition,
Institute for Medical Research,
50588 Kuala Lumpur
Malaysia

Printed by:

Academe Art & Printing Services Sdn. Bhd.,
Lot 14082, Jalan Kuchai Lama,
58200 Kuala Lumpur.

ORGANISING COMMITTEE

Executive Committee	Dr Chong Yoon Hin (President) Dr Mohd. Ismail Noor (Secretary-General) Dr Tee E Siong (Treasurer) Dr Tony Ng Kock Wai Mr Mohd Nordin Abdul Karim Ms Safiah Yusof Ms Jayamalar Chelladurai Ms Zanariah Jiman Dr Aminah Abdullah Dr Khor Geok Lin Dr Daniel T.S. Tan Ms Uma Rani Thevendran
Scientific Sub-Committee	Dr Chong Yoon Hin (Chairman) Dr Tony Ng Kock Wai (Secretary) Dr Mohd. Ismail Noor Dr Khor Hun Teik Dr Khor Geok Lin Dr Loke Kwong Hung Dr Aminah Abdullah Dr Zawiah Hashim Dr Wan Abdul Manan Wan Muda
Finance Sub-Committee	Dr Tee E Siong (Chairman) Ms Safiah Yusof (Secretary) Ms Shanaz Mawji Dr Mohd. Ismail Noor Ms Susan Wang Datin Mimi Hamzah Dr Zaitun Yassin Ms Siti Mizura Shahid
Social & Publicity Sub-Committee	Dr Mohd. Ismail Noor (Chairman) Mr Mohd. Nordin Abdul Karim (Secretary) Ms Rubiyah Jamil Dr Daniel T.S. Tan Ms Uma Rani Thevendran Ms Zanariah Jiman Ms Jayamalar Chelladurai Dr Zawiah Hashim Ms Nawalyah Abdul Ghani Capt Maznorila Mohd Ms Kalanithi Nesaretnam

CONTENTS

MATERNAL AND CHILD NUTRITION

NUTRITION AND AGEING

NUTRITIONAL TOXICOLOGY

NUTRITION AND CANCER

NUTRITION AND CARDIOVASCULAR DISEASE

ENERGY ADAPTATION AND OBESITY

IRON DEFICIENCY AND IRON DEFICIENCY ANAEMIA

NUTRITON IN TRANSITION (CHANGING DIETARY PATTERNS)

NUTRITION AND DIABETES

FOOD AND NUTRITION POLICIES IN NATIONAL DEVELOPMENT

VITAMINS AND MINERALS IN HEALTH AND DISEASE

FOOD INDUSTRIES AND NUTRITION

SPORTS NUTRITION

NUTRITIONAL ASPECTS OF EDIBILE OILS AND FATS

NUTRIENT COMPOSITION OF FOODS

CONTROL AND ELIMINATION OF IODINE DEFICIENCY DISORDERS

RAPID ASSSESSMENT PROCEDURES FOR THE EVALUATION AND IMPROVEMENT OF NUTRITION PROGRAMMES

DIETETICS IN ASIA - THE NEXT DECADE

ASSESSING, ANALYSING AND MONITORING CHANGES IN NUTRITION PROBLEMS

CHANGING NUTRITIONAL NEEDS IN THE WORLD TODAY

NUTRITIONAL EPIDEMIOLOGY IN THE ASIA PACIFIC REGION

SUB-THEME: BASIC ISSUES IN NUTRITIONAL EPIDEMIOLOGY

SUB-THEME: NUTRITIONAL EPIDEMIOLOGY TRAINING IN THE REGION

---

* Paper not submitted at time of printing.

Proc 6th ACN 1991: 1-20

Challenges and frontiers in nutrition in Asia

C Gopalan

The Nutrition Foundation of India, New Delhi, India

Asia today accounts for 59% of the total world population, and for an annual addition of 55 millions to it. The population of Asia is expected to exceed 3.5 billion by the year 2000 (1). Thus to speak of Asia is to speak of nearly two-thirds of Mankind.

To the students of demography and "development", Asia presents fascinating contrasts. It has within its borders, on the one hand, the two biggest countries of the world - China and India, which between themselves account for nearly 2 billion people today; and, on the other, some of the world's smallest states like Bhutan and Singapore. The countries of Asia, between themselves, also constitute a very wide spectrum on the economic developmental scale. Thus, while Asia can today boast of at least one of its countries being in the "Big League" wielding an economic strength that surpasses those of the countries of North America and Europe, it is unfortunately also the home of some of the poorest countries of the world.

Thus Asia and its peoples are by no means a homogeneous entity. The challenges that confront different Asian countries therefore are not all of the same order, nor indeed of the same kind. Most countries of Asia (except Japan) however come broadly under the category of "developing countries" and belong to the so-called Third World; and it is to this category of poor developing countries of Asia that many of the following observations will apply.

The background

In the ultimate analysis, the challenges which most developing countries of Asia face today, spring from their basic problems of poverty and population pressure. These countries started on their developmental journeys, as it were, nearly five decades ago, with a backlog of 'underdevelopment'. The prevailing inequitable International Economic Order has not generally been favourable for their rapid socio-economic development. The harsh "structural adjustments" they are presently being called upon to make, leave them little room for adequate investments in long - range developmental plans aimed at bringing about enduring nutritional upliftment of their populations. With an ever growing debt burden, and a good part of their external borrowings being swallowed up for servicing their earlier debts, they are often compelled to resort to policies largely aimed at no more than immediate survival. Programmes that would help mitigate the **symptoms** of undernutrition take precedence over those that would serve to attack its root **causes**. Land and water resources are often being improvidently used with the immediate needs for augmentation of food production, or industrialisation in the forefront, pushing considerations of long-term interests to the background.

During the last four decades, many Asian countries despite their economic weakness and rising populations have

achieved significant progress in health/nutrition. Mortality rates have been declining - more strikingly in some countries than others, and life expectancy has risen. Acute large-scale famines that used to decimate vast sections of populations in earlier years have been eliminated. Florid clinical forms of undernutrition like kwashiorkor, nutritional blindness, beri-beri and pellagra have declined substantially; but many formidable challenges still remain.

In a broad sense, the challenges, which the developing countries of Asia now face, and which have a direct bearing on nutrition, are of two kinds (Table 1). Firstly, there are the challenges that spring directly from their current state of poverty and undernutrition; and these relate to the long-standing 'old' problems of undernutrition which they have not as yet totally eradicated. Secondly, there are the 'new' challenges, which are emerging as a corollary of the very process of "development" which these countries are engaged in, as part of their efforts to improve their lot and achieve socio-economic advancement; and these largely relate to such by-products of the "developmental process" as environmental degradation, urbanisation, and demographic transition.

TABLE 1
Challenges in nutrition in Asia

Challenges related to 'old' problems

1. The immediate challenge
   Goitre, hypovitaminosis A and iron - deficiency anaemia
2. The challenge of the second phase

Emerging challenges related to "development"

1. Environmental degradation of land and water resources
2. Urbanisation
3. Ageing (demographic transition)

I. Challenges relating to "old problems"

1. The immediate challenge

An immediate and major challenge for Asian countries is the effective control, if not the eradication, within the next decade, of three specific problems of undernutrition - namely goitre, hypovitaminosis A, and iron-deficiency anaemia, - which have plagued them for centuries. The resources and the technology needed for this purpose are certainly available **within** these countries even today; the necessary political and administrative competence, however, need to be summoned. Control of these three problems within the next decade is a realistic and feasible target to aim at.

Some notes of caution need to be clearly sounded in this regard. In attempting the control of these diseases, developing countries of Asia should carefully avoid falling into the trap of opting for technologies which are not sustainable within their own means - technologies for the continued application of which they will have to be forever dependent on external donors. Relatively inexpensive, and proven technologies well within the means, resources and competence of

even the poorest countries of Asia are now available for the elimination of these problems.

Goitre

The inexpensive technology, a time-honoured and time-tested one, for the control of goitre, is iodation of common salt. Programmes for goitre control in Asia must squarely and solidly rest on this technology. Unfortunately the implementation of this strategy has been tardy and inefficient in several Asian countries. Either the salt is not properly iodated, or, adequate amounts of it are not made available in time to the needy populations, or, the programme is unfortunately (as in the case of India) allowed to run into needless controversies such as "universal iodation" versus "iodation limited only to endemic zones". These are deficiencies in **implementation** and not in the technology; these deficiencies must be resolutely overcome, and should not be allowed to be used as excuses or arguments for an alternative technolgy.

Asian countries currently beset with the goitre problem may do well to set up empowered National Goitre Commissions which can help to achieve inter-sectoral coordination and expeditious implementation of goitre control programmes as a unified operation with the mandate of achieving the eradication of the disease before the turn of this century. This is specially important as new endemic areas seem to be emerging in the irrigated plains of some Asian countries.

Periodic parenteral administration of iodation oil (not presently manufactured in any Asian country) has been suggested as an alternative approach, especially in areas "inaccessible" to common salt. I am not aware of any areas in Asia which are now "inaccessible" to common salt, but which will become easily "accessible" to iodated oil, to thousands of disposable syringes, and to an army of "injectors"! Asian countries will do well to pause and ponder ! Apart from the apprehensions in this regard which I had voiced earlier (2), and apart from the increased expense and the unnecessary drain on meagre foreign exchange resources that this approach would inevitably involve, it must also be remembered that Asian populations are now facing two major problems which could get compounded to disastrous proportions through the use of the periodic iodated parenteral administration of oil as a large scale public health operation, namely, the problem of AIDS and hepatitis. There has been a steep rise in the HIV sero-positivity rate among drug addicts of North East India during the last two years. Thus the data of the Indian Council of Medical Research show that half of the drug users in this region, which is also precisely the area highly goitre-endemic, were seropositive in 1990. Those familiar with real-life situations in the field, will realise that "disposable" syringes will not be dutifully "disposed"; under the circumstances, the consequences of resort to a technology which is dependant on repeated injections (using "disposable" syringes) could be disastrous. Prudence and national interests dictate that we resolutely stick to salt iodation, disregarding signals and sounds to the contrary.

Hypovitaminosis A

There has fortunately been a steep decline in the incidence of keratomalacia, the more serious form of vitamin A deficiency during the last few decades. However milder forms of vitamin A deficiency are still widespread.

The present strategy for the control of vitamin A deficiency is largely based on the periodic administration of massive oral doses (200,000 I.U) of synthetic vitamin A at six monthly intervals to children at risk. This strat-

egy was originally designed purely as a temporary expedient till such time as we were able to develop the logical approach of augmenting the intake of carotene-rich foods in the dietaries of our populations. What was originally designed as a temporary expedient has now continued for over 20 years and threatens to expand. The time has come for a careful review of this strategy partly because keratomalacia for which it was originally designed has steeply declined, partly also because of our present better appreciation of the limitations of this strategy, and most importantly because we have in Asia an abundance of natural food resources right at our own doorsteps, with which we can combat this problem.

Asian countries are fortunately blessed with a very wide array of relatively inexpensive foods rich in provitamin A carotenoids. There is also a vast, as yet, untapped potential for not only augmenting the production of such foods, but for the development of other carotene-rich food sources, like spirulina and red palm oil. It will be prudent for Asian countries to base their approach to combating vitamin A deficiency on the maximal use of these valuable indigenous inexpensive national food resource. Though during the last 20 years after the introduction of the periodic massive synthetic vitamin A dosage approach, we had frequently paid ritualistic lip services to "papayas, pumpkins and kitchen gardens", we had really not taken adequate practical steps to promote the use of green leafy foods. The challenge is to see that what we have preached so far at conferences is now put into practice in the field. Unless Asian scientists have permanently abandoned all hopes of ensuring vitamin A nutrition of their children through dietary improvement (for achieving which ample opportunities do in fact exist in their own countries) continued reliance on synthetic vitamin A makes no sense. The challenge now is to progressively discard the "magic bullet soft option" in favour of the logical approach of dietary improvement, within a reasonable time frame of 3 to 5 years. Present attempts to build periodic synthetic vitamin A administration into the Expanded Programme of Immunisation, as an integral part of it, are ill-conceived and uncalled for. This must be resisted. The challenge is to discard the "crutch" progressively and not to incorporate it as a permanent appendage.

Anaemia

Perhaps the most widespread, and yet the most neglected nutritional deficiency disorder in several Asian countries today is iron-deficiency anaemia. In recent years there has been substantial decline in the incidence of malaria and hookworm infestation in several developing countries of Asia; but there has been no significant dent in the problem of (primary) iron-deficiency anaemia. Iron-deficiency anaemia in pregnancy is an important risk factor, contributing to the high incidence of low birth weight deliveries in many Asian countries. The effective control of anaemia must rank as one of the major challenges. In view of the poor bioavailability of iron from cereal-based Asian dietaries, the control of this problem must depend on the administration of iron-folate tablets.

The weaknesses in the present strategy of iron-folate supplementation, responsible for the poor results obtained so far, need to be identified and corrected. It is generally believed that the poor outreach of basic health care services, on which the programme has to depend, is mainly responsible for the present failure. While this may be so, there are two other important aspects that need to be considered especially with respect to the control of anaemia of pregnancy.

1. A great majority (nearly two-thirds according to some data) of young adolescent girls of 6-14 years in the countries of the Indian subcontinent are anaemic; and in a considerable proportion the anaemia is of moderate or severe degree. These girls enter marriage in an anaemic state; and pregnancy only serves to aggravate preexisting anaemia. I had raised the question (3) as to whether the present strategy where iron-folate supplementation is limited to the last trimester of pregnancy will be adequate to reverse the anaemia under these circumstances; and whether it may not be appropriate to make iron-folate tablets freely available to all young girls in the countryside at least immediately after consummation of marriage, instead of waiting for the third trimester of pregnancy.

2. On the other hand, there is now increasing evidence pointing to the inhibitory effect of inorganic iron on zinc absorption (4,5). Iron therapy in doses generally prescribed in MCH care, is reported to have a measurable adverse effect on maternal zinc status (6). In view of the suspected widespread impairment of the content and bioavailability of soil zinc (and by inference poor zinc content of foods grown on them), on the one hand, and the reported effects of maternal zinc deficiency on the foetus on the other (7), this aspect needs careful investigation. As was pointed out earlier, placed as we are, iron-folate supplementation must be our mainstay for the control of anaemia; the question that needs to be examined however, is whether any precautionary steps would be necessary to prevent side effects, if any, following on intensive medication with iron in pregnancy.

Considering that anaemia is still a major problem in many Asian countries it is important that national and international agencies examine these issues in the light of available evidence and identify the most effective strategy for control of anaemia.

2. The challenge of the second phase

Eradication of famines, decline in incidence of florid nutritional deficiency diseases and better child survival belong to what may be called the First Phase of the battle against undernutrition. Developing countries of Asia have accomplished a good part of these major tasks of this early phase. However child survival cannot be equated with child health. We have now to think beyond child survival and eradication of florid deficiency diseases. Most Asian countries will soon be entering the Second Phase of their campaign against undernutrition, in which they will have to undertake the challenging task of ensuring the optimal nutrition of the "survivors". Stopping with the First Phase would result in no more than an expansion of the pool of substandard survivors and progressive erosion of the quality of the human resources of Asia. There is no half-way house in this journey.

In my earlier writings (8) I had referred to this as the "dangerous twilight stage" of development which msut be traversed expeditiously. Maurice King (9) would call it the "demographic trap". The answer certainly does not lie in slackening the drive for child survival (and conniving at, what Mahler (10) rightly condemns as an excercise in "mass euthanasia"); but in opting for a health policy which views child survival not as an end in itself, but as no more than an incidental by-product of our quest for optimal health/nutrition of our children as part of overall socio-economic development of the family and community. Our objective is not just that our children **survive**, but that they **live**, grow and develop into healthy, productive adults.

An **integrated** approach to Primary Health Care has been the general accepted policy of most developing countries of Asia. However, the zealous pursuit of isolated components of the integrated package as narrow vertical programmes - and the consequent crowding out of other components, has in recent years tended to distort this approach; and the benefit of synergism of mutually reinforcing components of Health Care which is the essence of the integrated approach is lost. If Maurice King's (9) rather provocative contribution helps to discourage this trend, it would have served some useful purpose.

Family planning

In order to traverse the second phase as expeditiously as they must, developing countries of Asia must overcome current deficiencies with respect to their family planning programmes. While these programmes have in recent years made headway, apart from China, in Thailand and Indonesia as well; and while Sri Lanka can boast of an excellent record, other countries especially those of the Indian subcontinent have sadly lagged behind. It is possible that too much reliance on just the propagation of contraceptive technology and too little attention to the social determinants of large family size among the poor has been responsible for poor results. Imaginative programmes aimed at universal female literacy; raising the age at marriage of girls, and promoting spacing of births; educational and vocational training beamed to rural adolescent girls (11); and towards active involvement of rural communities in health care - will need to be pursued vigorously. These latter approaches may have an impact on acceptance of family planning which earlier programmes directly attempting to promote contraceptive use have not had.

That Asian children, when freed of the environmental constraints on their growth and development can attain a level of growth corresponding to the international (WHO/NCHS) standards has been demonstrated by the experience of Japan. Recent studies in India (12) have also shown that affluent Indian children in some parts of the country have already achieved a level of growth comparable to the International standard. Growth retardation currently widely seen in Asian countries then is not a reflection of an inherent genetic trait; it is largely determined by environmental constraints imposed by poverty and deprivation.

Secular trend with respect to growth of children has however not been much in evidence among the poorer sections of populations of Asian countries. This is perhaps to be expected in the current stage of their development. A time-lag between the point of attaining a satisfactory level of child survival and the point of onset of a discernible secular trend in growth of the child population is perhaps to be expected, because the immediate effect of increased survival in a poor community could be a futher depression of the "average" level of growth. This again is an attribute of the "twilight phase". Real success of national nutrition upliftment programmes must be eventually reflected in improved growth performance of children of poor communities (not just of affluent sections). The state of Kerala in India has been (like the country of Sri Lanka) somewhat of a pioneer in the field of public health in Asia, and had achieved declines of infant mortality and birth rates of an order not achieved in the rest of South-East Asia. The latest surveys of the Indian National Nutrition Monitoring Bureau (13) seem to indicate that the secular trend even among poor population groups might have now started, at least in Kerala, the sentinel state of India. Perhaps, at

long last, we are seeing the light at the end of the tunnel!

It may be several decades before Asian children find full expression to their genetic potential for growth and development. Even prosperous Japan had taken over four decades. The major challenge for Asian countries in the next few decades is to ensure that this process of progressive unfolding of the full genetic potential for growth and development of their children, is promoted and expedited with all the inputs that will be needed for the purpose.

In singling out progressive increment in heights as a yard-stick of success, it is not implied that "tallness" is an end in itself. In an earlier publication I had adduced evidence pointing to the significance of "heights of populations as an index of their nutrition and socio-economic development" (14). Asian countries must firmly reject counsels of despair implicit in such defeatist slogans as " small is healthy" - "cultural adaptation " etc; which in effect attempt to condition us to a policy of "adjustment" to poverty rather than to one of combating and overcoming it.

II Emerging challenges related to "development"

1. Environmental degradation of land and water resources

The redeeming feature in Asia's overall food/nutrition situation has been that the continent in general is blessed with an abundance of land, water and natural resources, which, if properly harnessed, should enable most Asian countries to raise adequate food to meet the growing needs of their populations. Unfortunately, however, many developing countries of Asia, faced with the pressing need to use available land and water resources for their **immediate survival** and for rapid industrial development, had failed to bestow adequate attention to the conservation and judicious management of their precious land and water resources. Food/nutrition policies, and policies with respect to land and water use were apparently being largely dictated by short-term considerations which did not always keep long-term interests in view. As a result, developing countries of Asia today face what may well turn out to be the greatest challenge to the very foundation of their food/nutrition system - namely, a progressive erosion of the productivity of their precious land and water resources, on which the survival of their future generations will depend. It will be unfortunate, if it turns out, that in its anxiety to ensure its own immediate survival, the present generation of Asia, through improvident use of its land and water resources, had irreparably jeopardised the survival of future generations. The challenge now is to ensure that the process of environmental degradation is arrested through appropriate immediate remedial steps, and through more judicious and optimal use of land and water resources in future.

We may briefly review some major factors that have contributed to erosion of land and water resources in Asian countries.

Degradation of land resources

The major factors currently contributing to the erosion of land resources in developing countries of Asia have been diagrammatically illustrated in Figure 1. It is estimated that 25 billion tonnes of top soil are being lost annually from the world's crop lands (15). Asian countries are apparently making a significant contribution towards this enormous loss.

FACTORS CONTRIBUTING TO DECLINING LAND PRODUCTIVITY

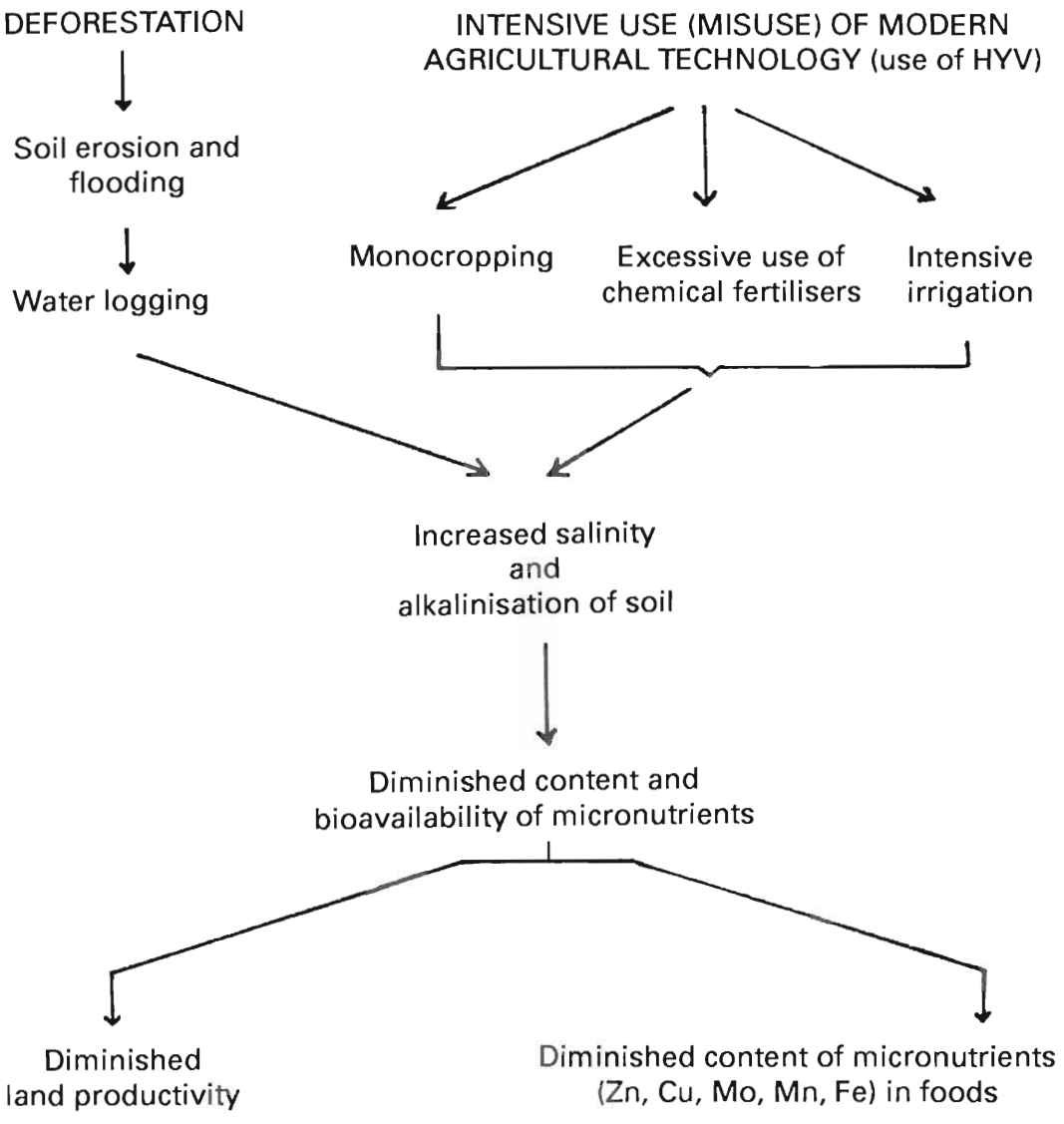


FIG. 1 Factors contributing to declining land productivity

Deforestation

Extensive deforestation has been ongoing in several countries of Asia such as Indonesia, India, Bangladesh, Myanmar, Thailand and Philippines for some decades. While it is heartening that in recent years attempts are being made to control the denudation and degradation of forests, these have not as yet generally yielded significant results. The deleterious effects of deforestation, soil erosion, flooding, water-logging, increasing soil salinity and alkalinisation, and diminished productivity have been far-reaching.

Unregulated use of modern agricultural technology

The use of HYV and consequential need for intensive irrigation and chemical fertilisers, had no doubt resulted in spectacular augmentation of food - grain production in Asia; but there are disturbing indications that the Green Revolution, might have extracted a heavy price ! The near-total jettisoning of organic manure, and or traditional systems of crop rotation and "slash and burn"; resorting to monocropping; the relative neglect of leguminous crops; - are all apparently contributing to a diminution in the content and bioavailability of important soil micronutrients, leading in turn to diminution of productivity of land, on the one hand, and impairment of micronutrient composition of foods grown on such depleted soils on the other. The deletrious effects on soil, of deforestation and ambitious irrigation projects, are being compounded by those of intensive agricultural technology.

The use of chemical fertilisers and pesticides in the countries of Asia has greatly increased in recent years. The fertiliser consumption in India, for example, which was less than a fraction of a million tonne in 1950, is expected to increase to 12 million tonnes by 2020 (16). Moreover, the fertilisers that are now being used, unlike the earlier ones, are refined, high-analysis fertilisers which do not contain most of the micronutrients and minerals that existed in the earlier ones as "impurities". Intensive cropping with the use of such high-analysis fertilisers could result in substantial loss of S, Fe, Mn, Zn and Cu. Unless these micronutrients are replenished, crop yields will progressively decline as indeed they have already started to do; for, after all, soil is not an inexhaustible source of such micronutrients. Inadequate use of organic manures and decreasisng proportion of legumes in the crop rotation are currently aggravating micronutrient efficiency in agricultural soils, and a spectrum of micronutrient deficiencies in soils appears to be emerging. Thus, according to a recent report, 53% of both soils and crops in Andhra Pradesh, 50% in Punjab and 64% in Haryana in India, have been reported to be deficient in zinc (16). These soils are also reported to show deficiencies with respect to Fe and Mn but of a lower order.

Agricultural scientists are already discovering that soil micronutrient deficiency is emerging as a major yield limiting factor. The far-reaching implications of such depletion of micronutrients in the soil, with respect to human nutrition have however not yet been fully appreciated.

Zinc deficiency

Zinc deficiency in soils and plants has particularly emerged as a possible major factor in the wake of intensive application of modern agricultural technology. Studies in Bangladesh (17) have revealed the possibility of poor content of zinc in a wide range of foods - fruits, vegetables legumes, grains, grasses and fodder crops. Zinc deficiency has been particularly noticed in rice crops grown on alkaline, wet and water-logged soils. These findings

could be of far-reaching importance to the nutrition of human populations in South-East Asian countries. Zinc is a vital component of such important metalloenzymes as carbonic anhydrase, peptidases, dehydrogenases and polymerases.

The possibility that deficiency of zinc could have far-reaching public health implications, and possible bearing on three of the major nutritional deficiency problems of South-East Asia - namely protein-energy malnutrition (PEM), hypovitaminosis A, and anaemia, has to be seriously considered. Zinc is a component of many key enzymes involved in protein synthesis. Zinc deficiency could therefore aggravate PEM and could be a factor contributing to growth retardation. Zinc deficiency could also induce reduction of RBP (retinol-binding protein) in plasma and liver, leading to poor mobilisation of hepatic vitamin A to the target tissues. Thus zinc deficiency may be a factor in the pathogenesis of hypovitaminosis A. The greater vulnerability of the rice crop to zinc deficiency could be reflected in poorer zinc nutritional status of rice-eating populations of Bangladesh and the eastern part of India; and this could partly explain the more pronounced endemicity of vitamin A deficiency in these regions rather than in the "wheat eating" western and nothern parts of India.

Degradation of water resources

Riverine and marine food resources are also apparently being steadily eroded. The growing threat to fisheries through environmental degradation must rank as a major challenge to several countries of Asia in the next few decades.

Floods and flood control measures

The construction of embankments, dams, and regulators across rivers have seriously impeded upstream and downstream migrations of fish from rivers and seas and lateral migrations into ponds, seriously interfering with ideal conditions necessry for fish breeding. In Bangladesh alone over 814,000 hectares have been claimed (18) to have become "flood-free" through such efforts; but these measures are also estimated to have resulted in permanent irreversible loss of 30,000 to 45,000 metric tonnes of fish every year. Fish has always been an important and relatively inexpensive source of nutrients for poor communities in river basins and coasts. The erosion of fisheries can thus seriously undermine the nutritional quality of diets in many poor households in Asia.

Industrial effluents

Industrial establishments in the Gangetic plains, and on the banks of Yamuna in India and on banks of other rivers in Bangladesh, are today causing havoc to fisheries. The culprits are a whole array of industries such as pulp and paper, textiles, tanneries, sugar distilleries, shellac, hydrogenated vegetable oils, coal washeries and petrochemicals. These industrial establishments are discharging pollutants which are contributing not only to considerable diminution of fish catch but also to hazardous metallic/toxic contamination of fish from such polluted sources.

The most notable metallic pollutants which pollute water sources in such Asian countries as India, Indonesia, Bangladesh and Thailand are mercury, lead, cadmium, copper, zinc and chromium; these heavy metallic contaminants not only persist over a long period but they are also generally water-soluble, non-degradable and strongly bonded to polypeptides and proteins. In addition human waste and untreated sewage discharged into the

rivers and the coasts also make their own significant contribution to the overall damage.

Pesticides

Pesticides used extensively in modern agriculture are also an important source of pollution of water sources because of their indiscriminate use; in this regard agriculture and aquaculture seem to be at cross-purposes. Much of the sewage from big cities bordering the coasts is being currently discharged untreated into the sea; and 65% of Asian cities each with populations exceeding 2.5 million are located along the coasts (19)!

The extent of loss of yield of fish, of poisoning of fish, and the extent of damage to human populations that such pollution is currently causing have not been quantified. Symptoms of poisoning are generally non-specific, and many cases go undiagnosed, especially, since most of the victims are drawn from the poorer sections of society. Since practically all the pollutants are powerful cellular poisons, impairment of nutritional status must be an important part of the overall impairment of the health status of these victims. The problems of undernutrition in poor Asian communities is thus being compounded by the problems of food contamination.

Damage to coastal ecosystems

It is estimated that by the year 2000 A.D. over 75% of the human population will be living in a narrow strip up to 60 km, along the shores of continents (19). More than two-thirds of Asia's population is currently living within 100 km distance from the sea. The coastal zones of Asia are thus today being subject to enormous population pressure. The denudation of mangrove forests, the degradation of coral reefs, the discharge of untreated sewage from coastal cities and towns and of effluents from urban industrial establishments, into the seas - are all adding up to a progressive dimunition in coastal and marine productivity and biodiversity (19).

Global warming

On the top of it all comes the alarming estimate that by 2030 A.D. there may be a rise of global mean sea level by about 18 cm (best estimate) as a result of global warming (19) - the "green house effect". This would imply that not just the fisheries, but the very existence of coastal cities and of the several cities of vast human populations inhabiting them, will be at stake, if energetic measures are not instituted to stem environmental degradation.

The challenge is to evolve policies that will help to ensure that effective environmental safeguards are built into developmental programmes in a manner that will not retard or hinder development. In order to achieve this, feasible, inexpensive environment - friendly technologies will need to be identified, and communities must be involved in their implementation.

2. The urban challenge

This has been truly the century of the "urban revolution". The countries of the Third World have witnessed massive urbanisation during the last four decades, with their total urban population soaring from 286 million in 1950 to 1.14 billion in 1990 (20). The data in Tables 1 and 2 may provide some indication of the formidable dimensions of the urban challenge confronting Asian countries. Of 22 cities of the world whose population is expected to exceed 10 million by the year 2000, as many as 13 will belong to Asia (Table 3). The urban challenge, as far as developing countries are concerned, is a growing challenge

because unlike in the case of the developed countries where the populations of large cities are expected to stabilise or even reduce, the process of urbanisation in Asia, Africa and Latin America will acquire even greater dimensions in the next few decades. More than a third of the urban populations in developing countries will be slum (or pavement) dwellers. Thus the urban population in India is expected to exceed 350 million by 2001 and of this over a 100 million will inhabit the slums (20).

TABLE 2
Estimated urban population in Asia 1950 - 2000

	1950	2000
Urban Population as percentage of total population (Asia)	16.4	35.0
Urban Population as percentage of total population (China)	11.0	25.1
Urban Population as percentage of total population (India)	17.3	34.2
Total Urban Population in Asia (in millions)	225.8	1242.4

Source: United Nations, Estimates and Projection of Urban, Rural and City Populations, 1950 - 2025: The 1982 Assessment (New York, January 1985).

Even as matters stand today, many urban centres of Asia are subject to major inadequacies with respect to water supply, sewage disposal, environmental sanitation, housing and transport. Even some capital cities in Asia currently do not have central waterborne sewerage systems and depend on septic tanks, cess-pools and pit-latrines for collection of waste, the effluents being discharged into storm-water drains without any pre-treatment whatsoever. Inefficient drains, high water tables and periodic flooding makes water pollution a major health hazard, and, as a result outbreaks of cholera and hepatitis among slum dwellers in major cities, are frequent. Factories located in the city outskirts discharge their toxic effluents into rivers and ponds, thus adding to the pollution of water sources. Overcrowding facilitates the spread of infections. Slums of big Asian cities are thus today fertile breeding grounds of communicable diseases. It is not surprising then that we are called upon to rely on ORT (Oral Rehydration Therapy) rather than improvement of environmental sanitation for the control of diarrhoeal diseases !

Rapid urbanisation at the present pace would inevitably impose enormous additional burdens. During the next two to three decades, there will be need for a two-to-three-fold increase in basic infrastructure, housing and living facilities in urban centres. The demands for clean water, sanitation, sewage disposal, schools, health sciences and transport will multiply enormously. The economic resources of the order that will be needed to meet this demand will be clearly beyond the means of many developing countries.

TABLE 3
Asian cities with populations exceeding 10 million in 2000 A.D.

City	Rank in 2000	Population in 2000 (in millions)
Tokyo	3	17.1
Calcutta	4	16.6
Bombay	5	16.0
Seoul	7	13.5
Shanghai	8	13.5
Delhi	10	13.3
Jakarta	13	12.8
Baghdad	14	12.8
Teheran	15	12.8
Karachi	16	12.2
Dacca	19	11.2
Manila	20	11.1
Beijing	21	10.8

Source: Integration of environmental consideration into city planning in intermediate cities by M.N. Buch - Asian Regional Conference on Urbanisation. Bogor, Indonesia 1991.

The emerging scenario would thus indicate that the problem of ill-health and undernutrition in urban slums of Asia could become formidable in the years ahead. Health systems of developing countries had so far (rightly) accorded higher priority (at least on paper) to rural health services in their developmental plans for the reason that rural populations far outnumber the urban ones, and generally have poorer access to health facilities. The urban sector may now need increasing attention and higher allocation of health-budgetary resources and indeed could consume a disproportionately large slice of national budgets. Urban slums because of overcrowding and high "insanitation-concentration" could act as reservoirs and fountain-heads of infectious outbreaks which will not necessarily be confined to urban slum populations alone. The concentration of microbial contamination in urban slums could frequently exceed the critical levels needed for epidemic outbreaks.

The changing occupation pattern of "working" women in urban slums could increasingly erode breast-feeding, and modify child-rearing practices. Studies by the Nutrition Foundation of India in three major cities of India - Bombay, Calcutta and Madras, nearly ten years ago (21) had revealed that breast-feeding practices in urban slums were in fact being seriously eroded - more so in some cities than in others; and commercial baby foods were being used increasingly (and unfortunately very improperly and unhygienically) for infant feeding. Comparative studies of rural and urban areas in earlier years had shown that in many cases, urban

children were nutritionally better-off than their rural counterparts. Apparently higher levels of income and better access to health facilities had had their beneficial effects. But with increasing overcrowding and insanitation in urban slums, this picture could change in the years ahead.

Asian countries will therefore need to develop imaginative policies to contain the growing challenge of urbanisation. Urbanisation cannot be arrested; but the pattern of urbanisation can be changed in a manner that will make the urban challenge less formidable and more manageable. These policies must be directed towards discouraging the overgrowth of large cities to unmanageable proportions, and towards favouring the growth of small and medium-sized towns which will help to ensure equity with respect to access to welfare and an equilibrium in which a few large settlements will not dominate the rest of the society (20). The policy must aim at a settlement system conducive for the generation of a continuous hierarchy of settlements ranging from village, small town, medium-size town, large city and metropolis. In such a scheme each settlement would serve a specific purpose and have a definite catchment hinterland with which it interacts, with both village and town, thus contributing to industrial prosperity. The rural - urban divide implicit in the concentration of urban populations in a few megacities will be avoided and national resources will be more equitably deployed and exploited. Problems of health and nutrition related to urbanisation will be minimised. Without such a policy, rural areas will be at increasing disadvantage with respect to services and policies, while urban slums will become major foci of communicable diseases and undernutrition.

3. Ageing and demographic transition

Practically all Asian countries struggling to achieve socio-economic development, have during the last few decades adopted policies for the containment of the growth of their populations. These policies implemented vigorously in some countries like, say, China, and less vigorously in certain others, have resulted in varying orders of declines in their birth-rates. With improved health care and better access to modern health technology, these countries have also achieved varying orders of decline in their mortality rates and increase in life expectancy. The declines in fertility and mortality are bringing about a demographic transition - speedier and more spectacular in countries which have been successful in achieving a significant decline in fertility and mortality, and less so in others. The dominant feature of this transition has been progressive ageing of their populations (Table 4).

In the developed countries of Europe and North America, the ageing process had been spread over nearly two centuries; because of this and because of their historic advantages, these countries had acquired a level of economic prosperity which enabled them to cope with the ageing problem, before the latter attained serious dimension. Even so, these countries are now discovering that the Utopia which they had hoped for with "successful" development and economic prosperity, had eluded them; and that they have also got into a "demographic trap" but of a different kind ! Indeed it appears that a number of them are now considering strategies for their self-rejuvenation - (pronatalist, immigration etc).

Developing countries of Asia will be in serious trouble if the proportions of old dependents in their populations

TABLE 4
Projected increase in population (in thousands)

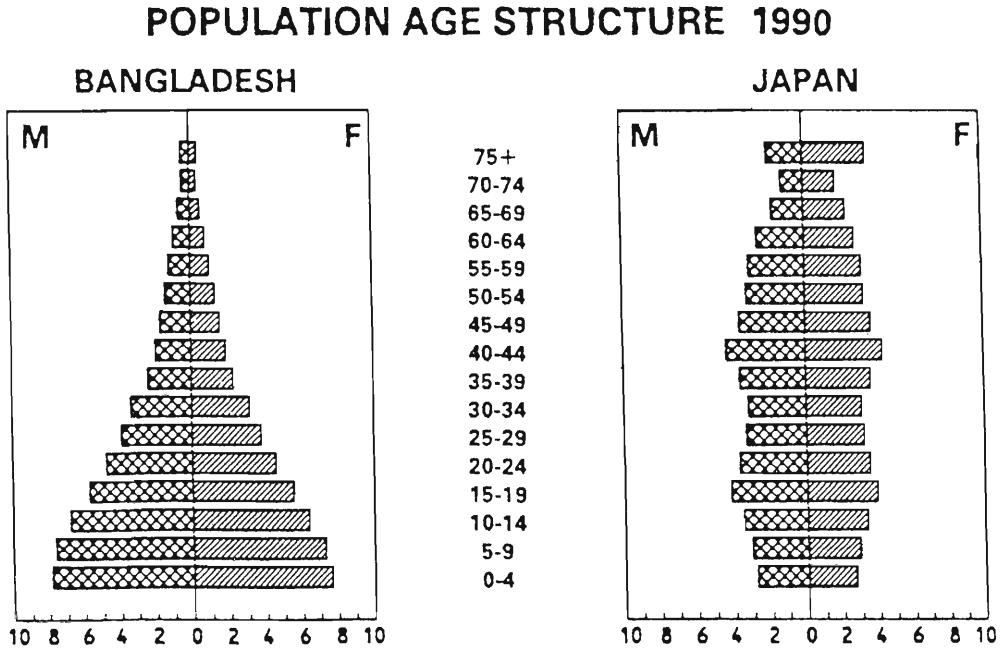
Countries	Increase in Total Pop. by 2050	Increase in Pop. > 60 yrs by 2050
Bangladesh	133586	13027
Bhutan	1870	173
Burma	46279	5292
DPR Korea	19664	112288
India	549330	23275
Mongolia	2275	325
Nepal	19316	1825
Sri Lanka	12029	3141
Thailand	43051	9849
Total	926222	172882

Source: Latest data (1990) from SEARO, WHO

reach high levels **before** they have been able to overcome their problem of poverty. The ageing process in Japan started in the middle of this century, and within a matter of less than five decades, Japan seems to have caught up with Europe. What took two centuries in Europe was accomplished in five decades in Japan. It is envisaged that by the second decade of the 21st century, the elderly (> 65 years) would outnumber the youth (< 15 years) and will constitute a quarter of the total population of Japan (22). But Japan has the economic strength to take care of the problem of ageing and escalating dependency ratio in its population. In China, the ageing process has been even faster, and had been set off at a rapid pace in 1970 when it adopted its "one-child policy". It is estimated that the population (> 60 years) which stood at 77 million in 1982 will rise to 298 million in 2025 amd 430 million by 2050 (23). China has thus a real problem on its hands. It is significant that there has been rethinking of the merits of the 'one-child-policy' and there is growing support for a less drastic "two-child" norm.

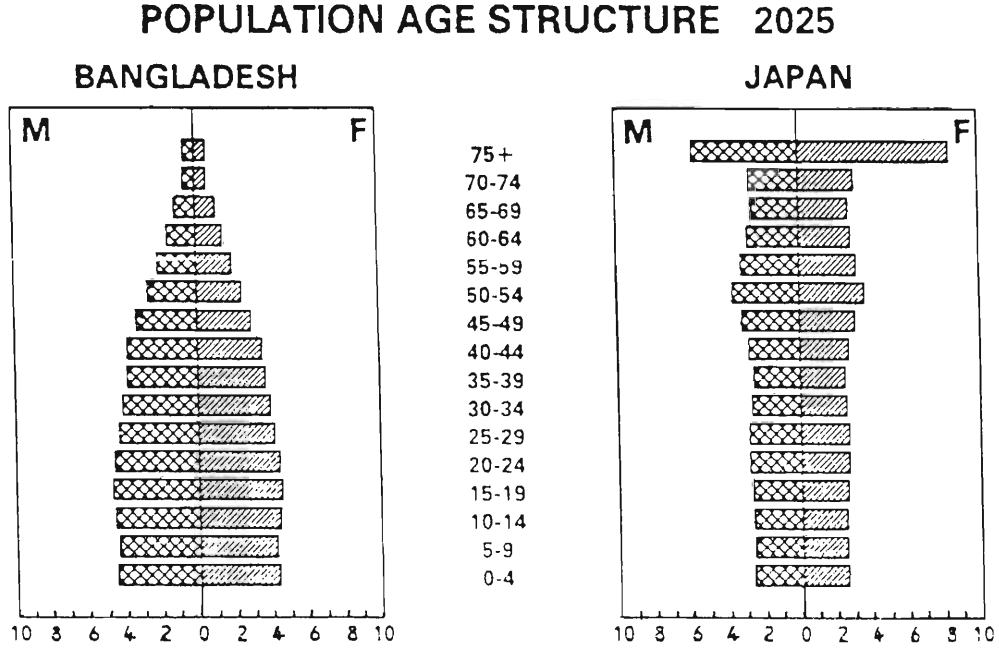
In the countries of South and South-East Asia where fertility control policies are being pursued with varying degrees of success, there are wide differences in the present age structures of populations (Figures 2, 3, & 4); the speed of the ageing process in these countries will also vary correspondingly.

It may however be shortsighted even on the part of poor developing countries of Asia to dismiss the challenge of ageing as a distant one. The challenge will increasingly come to the fore in the years ahead. While it is true that the average proportion of the elderly (> 60 years) will escalate only to around 12% by 2050 in the poorer countries of Asia (24), in absolute terms the number of the elderly in these countries will rise by about 175 million (Table 5). Policies to cope with the ageing process consistent with the resources and needs of these countries must be evolved.



Source: Asia Region Population Projections 1990-91, World Bank Working Paper WPS-599

FIG. 2 Population age structure 1990



Source: Asia Region Population Projections 1990-91, World Bank Working Paper WPS-599

FIG. 3 Population age structure 2025

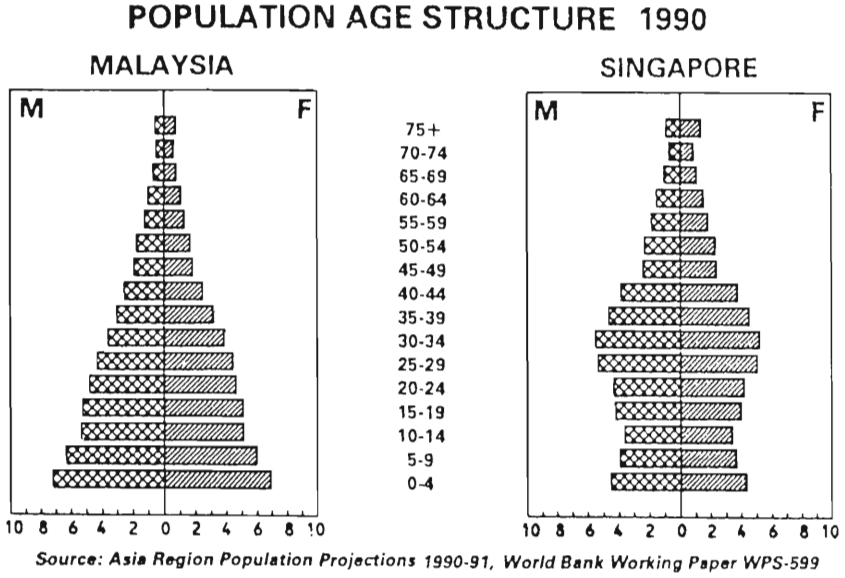


FIG. 4 Population age structure 1990

TABLE 5
Estimated and projected population above 60 years in South East Asia Region (in thousands)

Countries	1980	2000	2050
Bangladesh	3792 (4.30)	6504 (4.38)	16819 (7.58)
Bhutan	65 (5.02)	110 (5.42)	238 (7.52)
Burma	2155 (6.11)	3671 (6.66)	7447 (9.13)
DPR Korea	1028 (5.75)	1912 (7.02)	4715 (12.55)
India	33936 (4.96)	65655 (6.83)	146224 (11.85)
Indonesia	8012 (5.41)	14908 (7.50)	31287 (12.67)
Mongolia	84 (5.03)	174 (6.48)	409 (10.37)
Nepal	719 (5.03)	1276 (5.67)	2544 (7.57)
Sri Lanka	943 (6.37)	1800 (8.54)	4084 (15.21)
Thailand	2330 (4.95)	4496 (6.55)	12179 (13.52)

Figures in brackets denotes percentages.
Source: Latest Data (1990) from SEARO, WHO.

The problems posed by ageing of populations will have an important bearing on **all** sections of the society - children, working adults and family. Reordering of priorities with respect to social security and health care, and employment (retirement), will become necessary. Family structures and value systems will come under increasing pressure. How far would it be possible for shrinking working adult populations to sustain and support an ever expanding "elderly" population segment; to what extent, and for how long, would it be possible for extended families in Asian societies to take care of the growing numbers of elderly dependents in consonance with their established traditions; and what should be the nature and order of state-sponsored "collective arrangements" that would become necessary; what would be a reasonable allocation of health care/welfare "development" budgets as between children, on the one hand and the elderly on the other - say as between schools and old-age homes ? These are some of the agonising questions which policy-makers and planners of Asian Countries may have to grapple with in the next two decades. These are questions which cannot be evaded for long.

In developing countries of Asia, the problem of ageing will call for specific action (Table 6) in the following areas:-

(1) Health welfare and employment programmes for sustaining physical stamina and productivity of at least the populations in the 60 to 70 years age group so that they earn at least a part of their livelihood on their own. This will call for special arrangements with regard to health/nutrition care of the "old" age group.

(2) Since Asian dietaries are predominantly cereal-based and since with reduced calorie intake, these dietaries could become marginal or deficient with respect to protein, vitamins and minerals, special programmes for nutritional support to the poor "elderly" will become necessary.

(3) Elderly women will have to be treated as a specially "vulnerable" group, for the reason that: (a) because of relatively longer life-expectancy they are likely to outnumber elderly men, and (b) with increasing urban migration of able bodied youths, increasing number of destitute women will be "stranded" in villages. It is estimated that even, as of now, nearly two-thirds of single households in India are composed of women though single households represent just 6.5% of all households in the country (25).

(4) Evolving a system of care for the aged which reflects Asian traditions of parental care and extended families,

TABLE 6
Strategies for coping with the problem of ageing

1. Sustaining productivity of the Aged (at least 60 - 70 years age group)
2. Special attention to Elderly Women - a speciality vulnerable group
3. Ensuring nutritive value of dietaries in the context of reduced calorie intake
4. Encouraging family support to the Aged in preference to State sponsored Collective Support
5. Encouraging development of geriatrics as a Public Health Specialty

as well as the compulsions of the modern era - a system which provides encouragement and support (through tax concessions and allowances) to families supporting elderly parents on the one hand, and also support through state-sponsored "collective arrangements" like old age homes etc on the other.

(5) Developing geriatrics as an important speciality in the medical curriculum and the setting up of geriatic clinics in hospitals and health centres for prompt health care to the aged.

Concluding comments

Developing countries of Asia thus today face formidable challenges. But Asia is also fortunate in many ways; and, as the saying goes, we must not fail to "count our blessings".

While Asian countries face many handicaps, they also enjoy some inherent advantages. The challenges which even poor countries of Asia face today are much less arduous and exacting than those confronting some of the unfortunate countries of Africa. Asia unlike several parts of Africa, has land, water, and food resources within its borders, which if properly harnessed and managed should be adequate to meet practically all the food needs of its populations. The institutional infrastructures, the material / manpower / natural resources, which are available within Asia are no doubt currently inadequate to meet the demands of its growing populations and are also not being effectively deployed presently. Asia is certainly not starved of technical talent, despite the fact that much of it currently gets "exported". Asia can stand on its own feet. The challenge is, to enable it to do so.

References

1. Asia Region Population Projections (1990-91), World Bank Working Papers, WPS 599.
2. Gopalan C. Prevention and Control of Endemic Goitre. Special Publication Series No. 3, Nutrition Foundation of India 1987; 344-348.
3. Gopalan C. Control of Anaemia, Nutrition Foundation of India, Bulletin Vol 12, No. 2, 1991.
4. Solomons NW and Jacob RA. Studies on bioavailability of zinc in humans: effects of heme and nonheme iron on the absorption of zinc. Am J Clin Nutr 1981; 34: 475-482.
5. Valberg, LS, Flanagan PR, Chamberlain MJ. Effects of iron, tin and copper on zinc absorption in humans. Am J Clin Nutr 1984; 40: 536-541.
6. Hambidge KM, Kerbs NF, Sibley L and English J. Acute effects of iron therapy on zinc status during pregnancy. Obst Gynaecol 1987; 70: 593-596.
7. Mukherjee MD, Sandstead HH, Ratnaparkhi MV, Johnson LK, Milne DB and Stelling HP. Maternal zinc, iron, folic acid and protein nutriture and outcome of pregnancy. Am J Clin Nutr 1984; 40: 496-507.
8. Gopalan C. The changing profile of undernutrition in India. NFI Bulletin Vol 12 No. 1, 1991.
9. King M. An anomaly in the paradigm The demographic trap UNICEF's dilemma and its opportunities. NU Nytt om U - landshalsovard (News on health care in developing countries), 1991; Vol 5 1: 91.
10. Mahler HT. A humane way to help the world - NU Nytt om U - landshalsovard (News on health care in developing countries), 1991; Vol. 5 1: 91.

11. Gopalan C. The Female Adolescent (Mother to be): The key to Nutritional Upliftment and National Development. Nutrition Foundation of India Bulletin, Vol. 5 No 1, 1984.

12. Nutrition Foundation of India. Growth Performance of Affluent Indian Children (Under - Fives). Scientific Report 10, 1991.

13. National Nutrition Monitoring Bureau (1988 - 1990). Report of Repeat Surveys, National Institute of Nutrition, Hyderabad.

14. Gopalan G. Heights of Population - An index of their Nutrition and Socio - Economic Development. NFI Bulletin Vol. 8 No. 3, 1987.

15. UNEP (United Nations Environment Programme). The State of the World Environment, 1991.

16. Kanwar JS. Inaugural address at Micronutrient workshop, Andhra Pradesh Agricultural University, Andhra Pradesh, India, 1990.

17. Bangladesh Agricultural Research Council. Zinc in nutrition. Edited by Abdul Mannan and Abdul Rahim, 1988.

18. Ali M Yousouf. Environmental alterations deplete fisheries. Bangladesh Environmental Newsletter, Bangladesh centre for Advanced Studies, 1991.

19. Swaminathan MS. Human influence and evolution of the demography in the coastal zone. UNESCO conference on coastal systoms, studies and sustainable development, 1991.

20. Buch MN. Integeration of environmental considerations into city planning in intermediate cities. Proceedings of Conference on Urbanisation in Asia, Bogor, Indonesia, 1990.

21. Nutrition Foundation of India. Maternal Nutrition Lactation and Infant Growth in Urban Slums. Scientific Report 9, 1988.

22. United Nations. Social and Economic implications of Ageing Population (Annex). Report on Proceedings of International Symposium on Population structure and Development, Tokyo, 1988.

23. Banister J. Implications of the Ageing of China's Populations - Changing Family Structure and Population Ageing in China - A Comparative Approach. Ed: Zeng Yi, Zang Chunyuan, Peng Songjian, 1990.

24. SEARO. Latest data from WHO, 1990.

25. Bose A. Concern for Ageing Population - Populations to people, Volume II: 483 - 514, 1983.

Proc 6th ACN 1991: 21-41

Nutrition in transition: lessons from developed countries

Mark L Wahlqvist

Department of Medicine, Monash University, Prince Henry's Hospital and Monash Medical Centre, Clayton 3168, Melbourne, Victoria, Australia

Models of transition

Although it is the majority cultures of developed countries that receive most attention in so far as the impact of industrialisation on health outcomes is concerned, indigenous populations of countries previously subject to colonisation are usually affected to a greater extent (26) (Table 1). These populations often remain in transitional state between their traditional lifestyle and the city, in what is described as a "periurban" lifestyle. By comparing these groups it has become clear that the impact of urbanisation is progressively unfavourable on such peoples (4, 38) (Figure 1). Presumption has been that urbanisation will have been principally unfavourable to the majority of populations who live in such cities as well. However, comparisons between urbanised communities in different parts of the one nation or from nation to nation reveal that there must be many other factors which interact with urbanistion to affect health outcome.

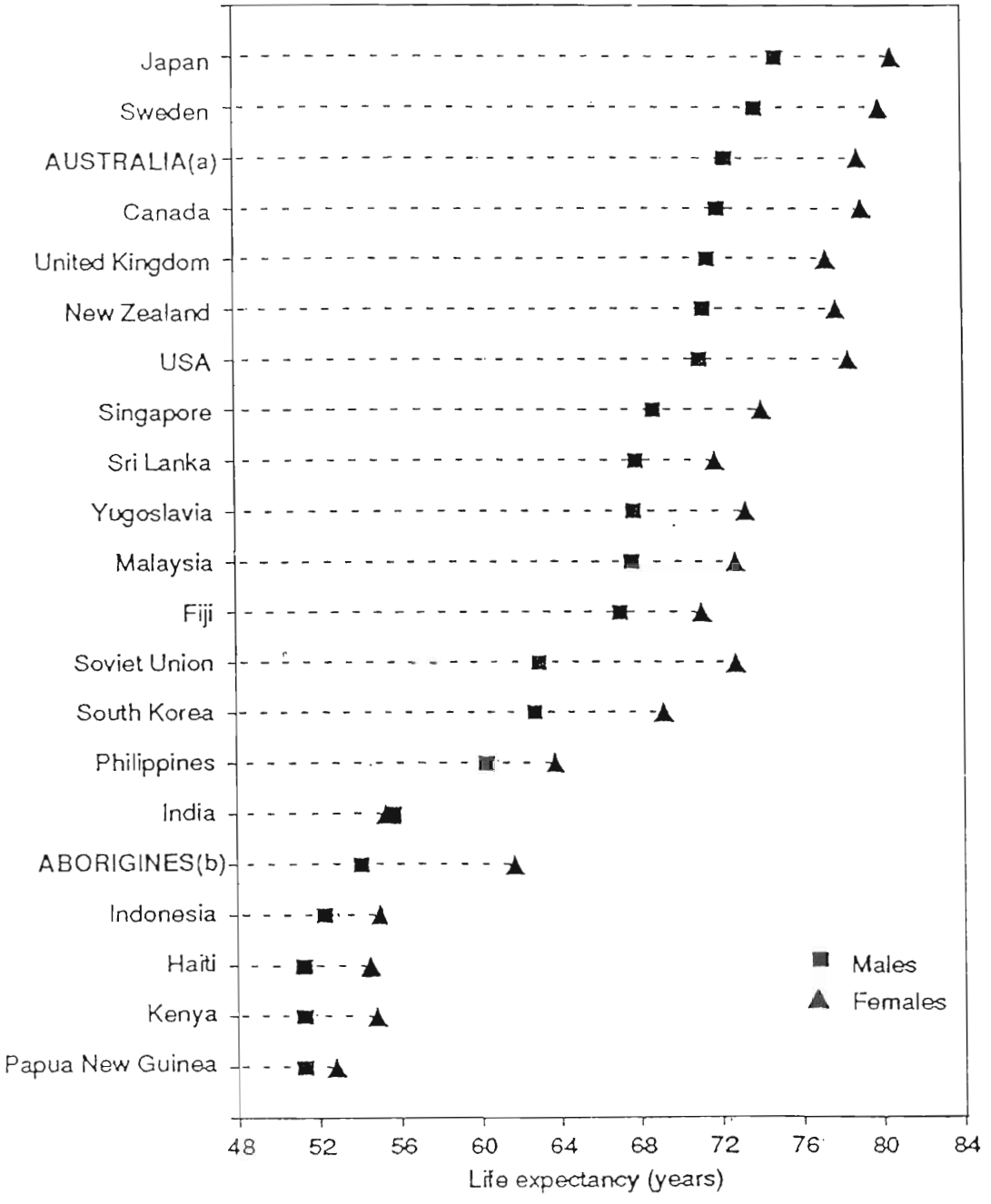
Immigrant populations, both old and recent, allow for a further disssection of some of the questions about food intake and health outcome with progressive societal change (40, 42, 48). Changes in food intake and colorectal cancer rates amongst immigrants to Australia are such an example (32, 42) (Table 2, Figures 2a, 2b).

Food culture is composite of many variables and there has been a particular need to develop cross-culturally robust methodologies for nutritional status and health status (25). Studies now underway within and between countries of different cultural groups are shedding important light on food health relationships (19).

It seems likely that significant common denominators for difference in nutritionally related health outcomes between communities, and with the passage of time, include both **education** and **socio-economic factors** (16). As educational and socio-economic status improve, so also does

TABLE 1
Models of Transition in Developed Countries

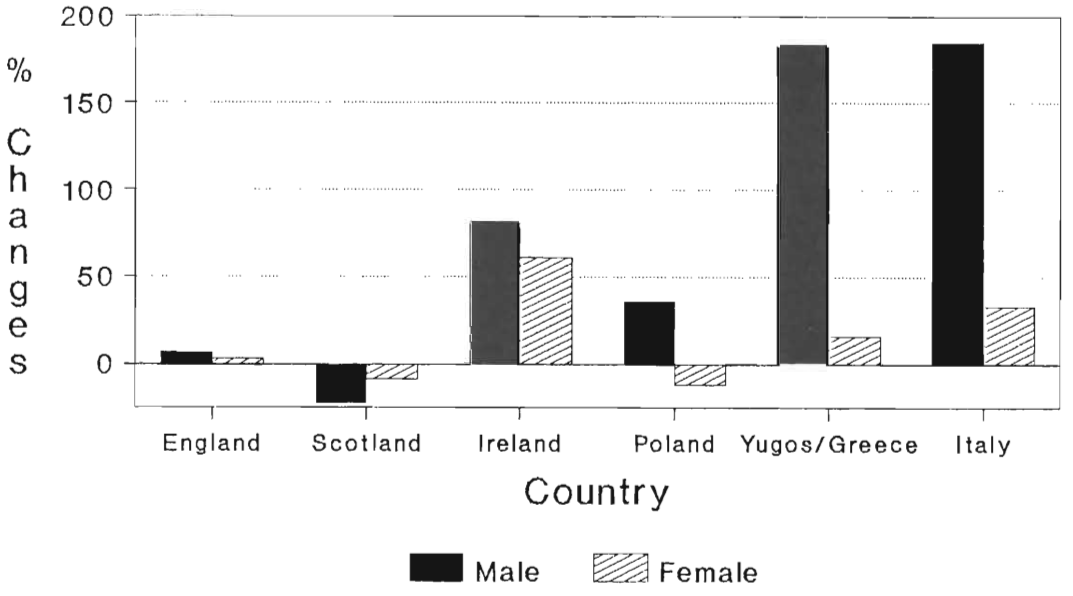
1. Indigenous populations
2. Urbanisation
3. Immigrant populations
   (1) Old immigrant
   (2) Recent immigrant
4. Cross-cultural comparisons
5. Educational and socio-economic differentials
6. Age dependency



(a) Includes Aborigines and Torres Strait Islanders
(b) Includes Torres Strait Islanders

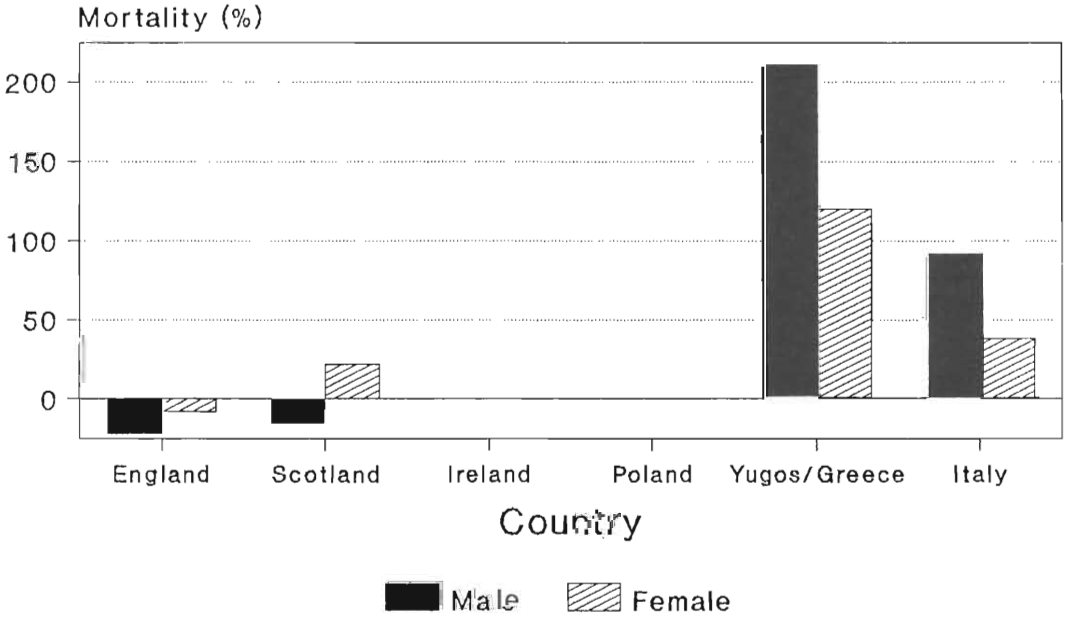
Source: United Nations 1987
Australian Bureau of Statistics 3302.0

FIG. 1 Life expectancy at birth for Aborigines and selected countries, 1985.



McMichael et al., 1980

FIG. 2a % changes in colon cancer mortality between short term (<16 years) and long term (<16 years).



McMichael et al., 1980

FIG. 2b % changes in rectal cancer mortality between short term (<16 years) and long term (>16 years).

TABLE 2
Foods and beverages for which consumption differed by 5% or more between Greek migrants resident in Australia for shorter (<16 years) and longer (>16 years) periods

Food Item	Percent consumption by long-stay group and difference from short-stay group (in brackets)	
	Males	Females
Cereals		
Pasta dishes	12(-5)	13(0)
Milk and Milk products		
Cheese	56(-9)	65(+6)
Meats		
Pork, Ham and Bacon	36(+11)	12(+2)
Vegetables		
Potatoes	39(-3)	36(-5)
Pulses	15(+6)	8(+2)
Wild leafy greens	10(-4)	10(-5)
Beverages		
Tea	45(+15)	51(+18)
Soft drinks	32(+5)	25(+1)
Beer	28(-6)	8(-2)
Wine	26(-5)	12(-6)
Water	16(-5)	24(-3)

Source: Rutishauser IHE & Wahlqvist ML. Proc Nutr Soc Aust 1983; 8:49-55

food variety. Diseases which are putatively, nutritionally - dependent like diabetes and cardiovascular disease are also related to social class ratios (Table 3 and Figure 3).

It is also clear that one of the most significant confounding variables in a consideration of transitional societies and their health is **age**. Whilst there is a great deal of homogeneity about biological age for a given chronological age in childhood, such is not the case in later life. Thus the elderly in an indigenous population like that of peri-urban Aboriginal Australians are younger in chronologicl age than those of Caucasians in the same country. At the moment, the methodological ability to take account of chronological age exceeds that for biological age (51).

Dietary tolerance

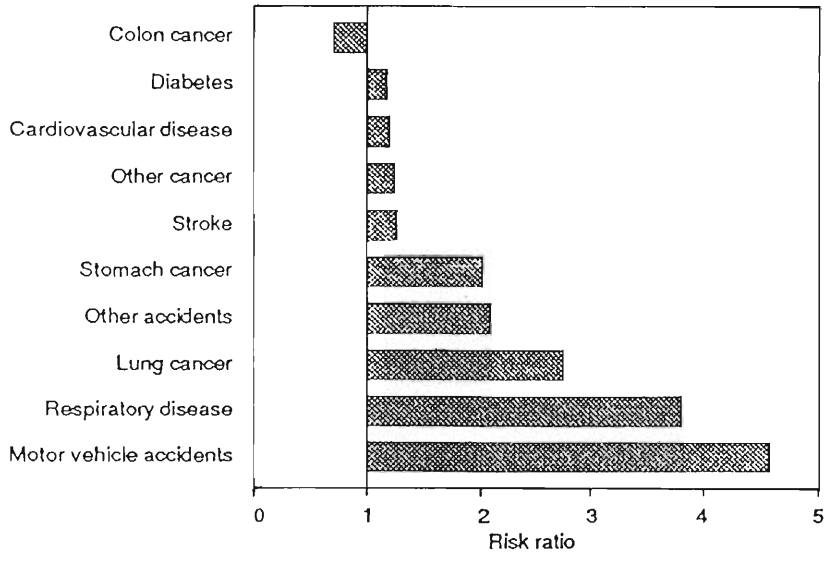
Although food intake may be in transition from one pattern to another, its impact on health status will depend on tolerance to change. This is a familiar concept with functional reserve

TABLE 3

Effects of education and socio-economic status (occupation and income) on food variety amongst Melbourne Chinese

	Men		Women	
	"BV"	"PV"	"BV"	"PV"
Education (yr)				
0-6	69.7	38.5	73.1	42.6
7-9	77.4	45.9	75.7	45.6
10-12	78.1	47.7	81.1	50.9
13+	84.9	56.3	85.1	58.2
Significance level	*****	****	****	****
Occupational status				
Professional/ administrative	84.6	56.8	85.1	57.5
Clerical/sales	80.1	50.9	78.8	49.3
Trades/services	76.8	46.3	77.0	46.4
Home duties	76.7	41.2	75.1	45.5
Significance level	****	****	****	****
Income (AU$ PA)				
0-12,000	76.3	44.5	76.2	44.7
12,001-22,000	75.6	44.6	77.1	45.8
22,001-40,000	79.1	49.0	78.6	49.9
40,001-	85.0	57.1	82.3	54.6
Significance level	****	****	****	*

NS, not significant;*, p<0.05; **, p<0.01; ***, p<0.001; ****, p<0.0001.
"BV" is biological variety; "PV" is product variety
Source: Hage & Wahlqvist, unpublished data



(a) Ratio of age standardised death rate for lowest social class to age standardised death rate for highest social class. Social class defined by using Congalton 4-point scale classification of occupation.

Source: McMichael 1985

FIG. 3 Social class risk ratio (a) for selected causes of death, males, 1970.

capacity in organs like the heart when one is considering, for example, the impact of unplanned physiological stress or of myocardial disease. The measurement of variation in food intake and how it relates to health outcome is in its infancy. Food variety is one such approach (Tables 3A, 4). A recent paper and editorial in the New England Journal of Medicine on Variation in Energy Intake in Children and the extent to which it comes out on target over weeks is illustrative of this point (5, 12, 15). What is more is that the ability to make these adjustments in energy intake might ultimately be a predictor of energy imbalance reflected in obesity. Perhaps related to this consideration is the emerging application of CHAOS Theory to human biology (18, 24). Apparent disorder may well be a marker of health.

Models for enquiry into dietary tolerance will include those of intra-individual variation, of intra-cultural difference (which otherwise might be regarded as inter-individual difference) and inter-cultural difference.

Favourability and unfavourability of transition.

Transition may result in both favourable and unfavourable outcomes. Throughout the twentieth century, food cultures in almost every country have been undergoing radical change, with only the more remote and isolate maintaining high degrees of traditionality. Within Europe, the advent of the European Economic Community (EEC) has made major inroads on the food traditions of southern Europe. The progressive introduction of western food tech-

TABLE 3A

Food variety as a determinant of cardiovascular risk in Melbourne Chinese women (48)

	"Biological variety"			"Product variety"		
	b	*(se)*	*p*	*b*	*(se)*	*p*
SBP(mmHg)	-0.49	(0.12)	****	-0.41	(0.10)	****
DBP(mmHg)	-0.069	(0.059)	NS	-0.052	(0.048)	NS
CHOL(mmol/l)	-0.015	(0.0064)	*	-0.014	(0.0052)	**
TRIG(mmol/l)	-0.0093	(0.0045)	*	-0.0077	(0.0037)	*
HDLC(mmol/l)	0.0041	(0.0021)	NS	0.0031	(0.0017)	NS
LDLC(mmol/l)	-0.014	(0.0058)	*	-0.013	(0.0047)	**
LDL/HDLC	-0.017	(0.0052)	**	-0.015	(0.0042)	***
BMI(Kg/M^2)	-0.027	(0.018)	NS	-0.036	(0.014)	*
Waist to ratio	-0.0015	(0.00043)	***	-0.0012	(0.00035)	****
Fasting glucose (mmol/l)	-0.025	(0.0086)	**	-0.020	(0.0070)	**

NS, not significant; *, p<0.05; **, p<0.01; ***, p<0.001; ****, p<0.0001
Source: Wahlqvist, Hage, Powles, Oliver & Balazs, 1991

TABLE 4
Food variety and arterial wall characteristics (diabetics and healthy) all subjects (50).

	Total	Plant
A-l compliance	0.38**	0.31*
P-W damping		
Common femoral	-0.38**	-0.31*
Posterior tibial	-0.44**	-0.41**

* $p<0.05$; ** $p<0.01$
rs is Spearman's rank correlation efficient; AL is aorto-iliac; P-W is pulse wave.
Source: Wahlqvist, Lo, Myers, 1989; ref (50)

nology into China represents the beginnings of significant change in Chinese food habits. The surge of development in food technology in Japan is on the threshold of making major shifts in thinking and will blur the occidental categorisation of food as food and medicine as medicine, since this has never been a sharp distinction in oriental thought.

For all of these major changes in food production, supply routes, processing, and family eating traditions in recent decades, overall life expectancy has, in general, improved. This probably reflects a progressive identification of those aspects of food consumption favourable to health. It also simply reflects a more abundant food supply, so that less starve or suffer from specific nutrient deficiencies. What is less clear is how the myriad non-nutrient components of food, also now available in abundance through a greater and more diverse food supply have favourably contributed to our life expectancy and health.

Some health problems have increased as others have decreased. Good examples are the increase in colorectal cancer as gastric cancer has decreased (32). Since the increase in colorectal cancer is probably due to a separate set of dietary factors which were responsible for the expression of gastric cancer in the past, there is a considerable prospect of retaining the gains whilst addressing the new nutritionally related health problem.

Amongst the most impressive trend disparities have been the changing rates of coronary heart disease in different countries (2) (Figures 4 and 5) and in cancer deaths (Figures 6 and 7). On the other hand, both insulin dependent (41) and non-insulin dependent diabetes (54) appear to be on the increase in most places (17) (Table 5).

Unlike selective pharmacotherapy, food has the propensity to favourably influence health on several fronts at the same time such as cardiovascular disease, neoplastic disease, and, diabetes and osteoporosis. To understand these possibilities, it is necessary to understand the relationships between food patterns and disease patterns (47).

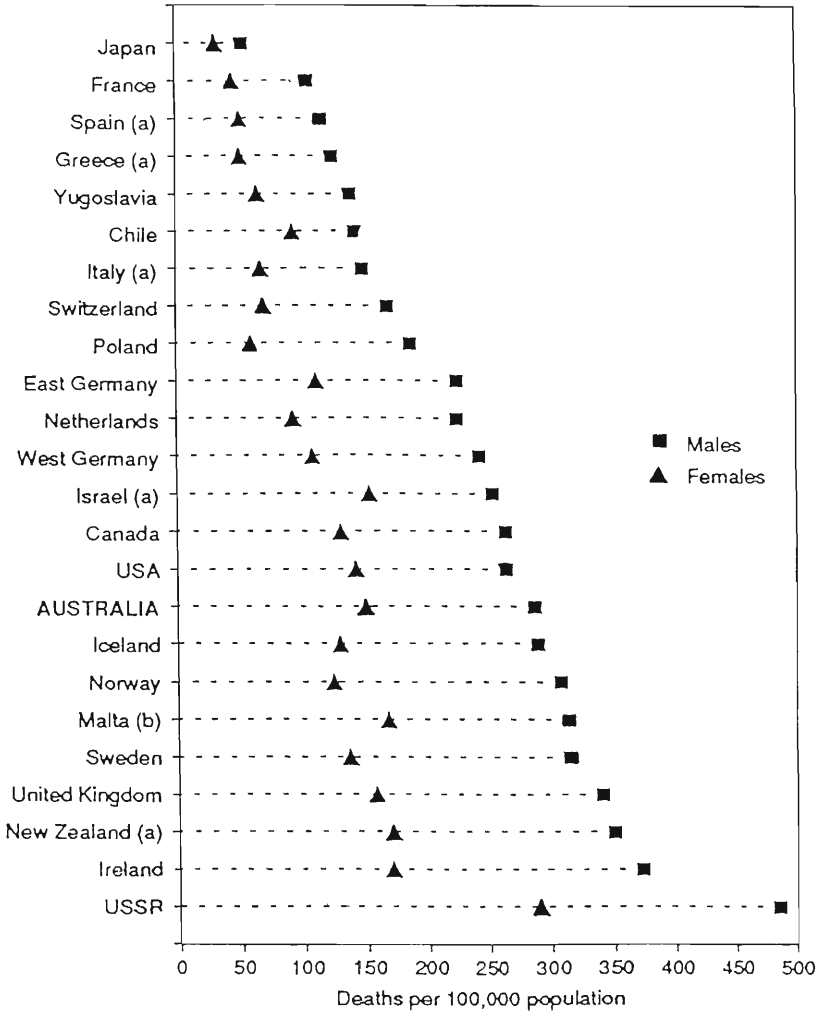
Admixture of under-and over-nutrition

When we speak of under-nutrition, we generally refer to protein-energy malnutrition, although we may also refer to specific nutrient deficiency. By

TABLE 5
Prevalence of abnormalities of glucose tolerance
Australian non-aboriginals Standardised for age over 25 years

	1966 (Busselton)	1981
Impaired glucose tolerance		2.9%
Known diabetes	1.3%	2.5%
All diabetes	2.2%	3.4%

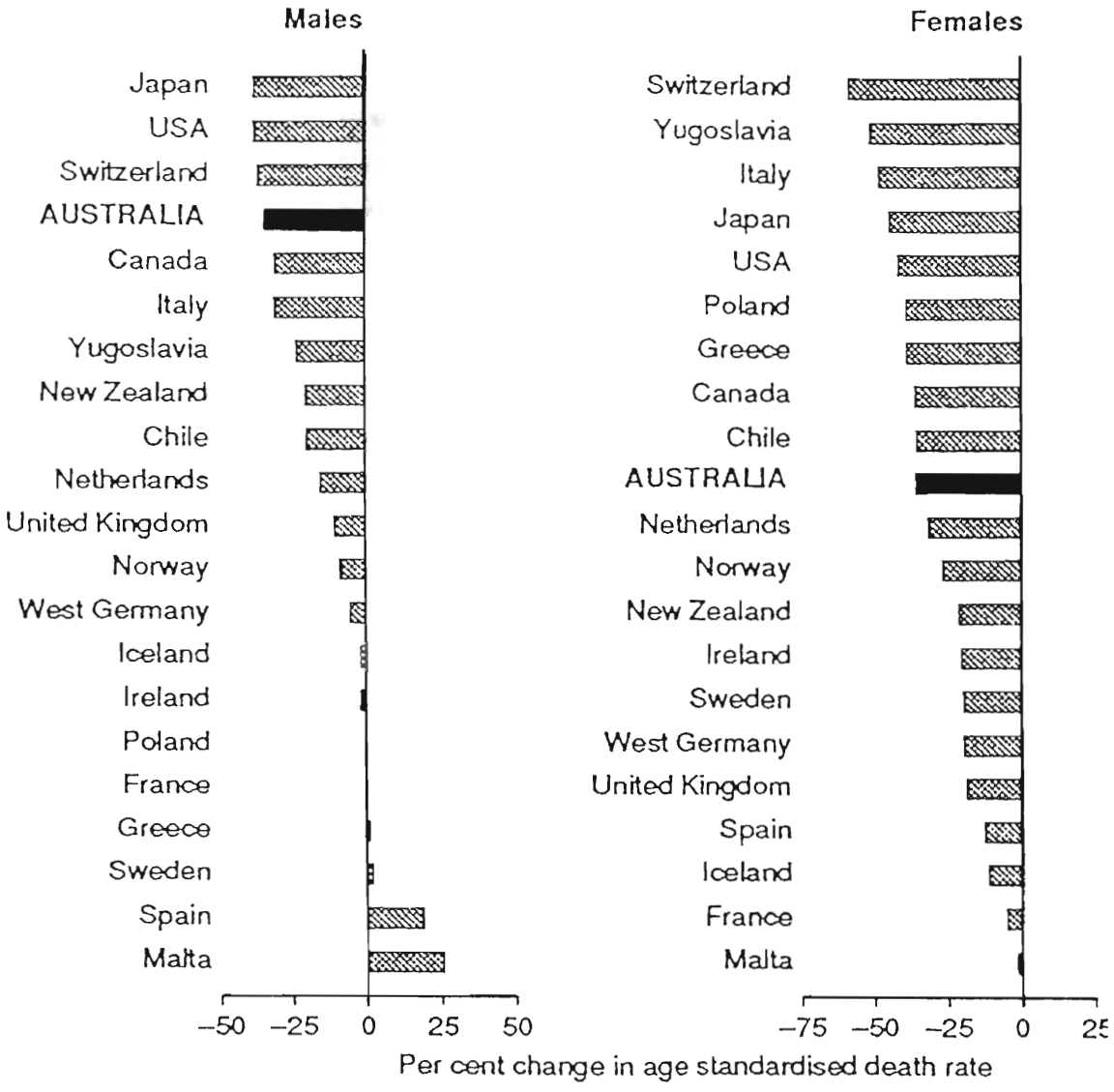
Source: Glatthaar C, Welborn TA, Stenhouse NS, Garcia-Webb P. (1981). Ref. (17).



(a) Greece, Italy, Israel and New Zealand 1986, Spain 1985
(b) Malta interpolated from 1986 and 1988

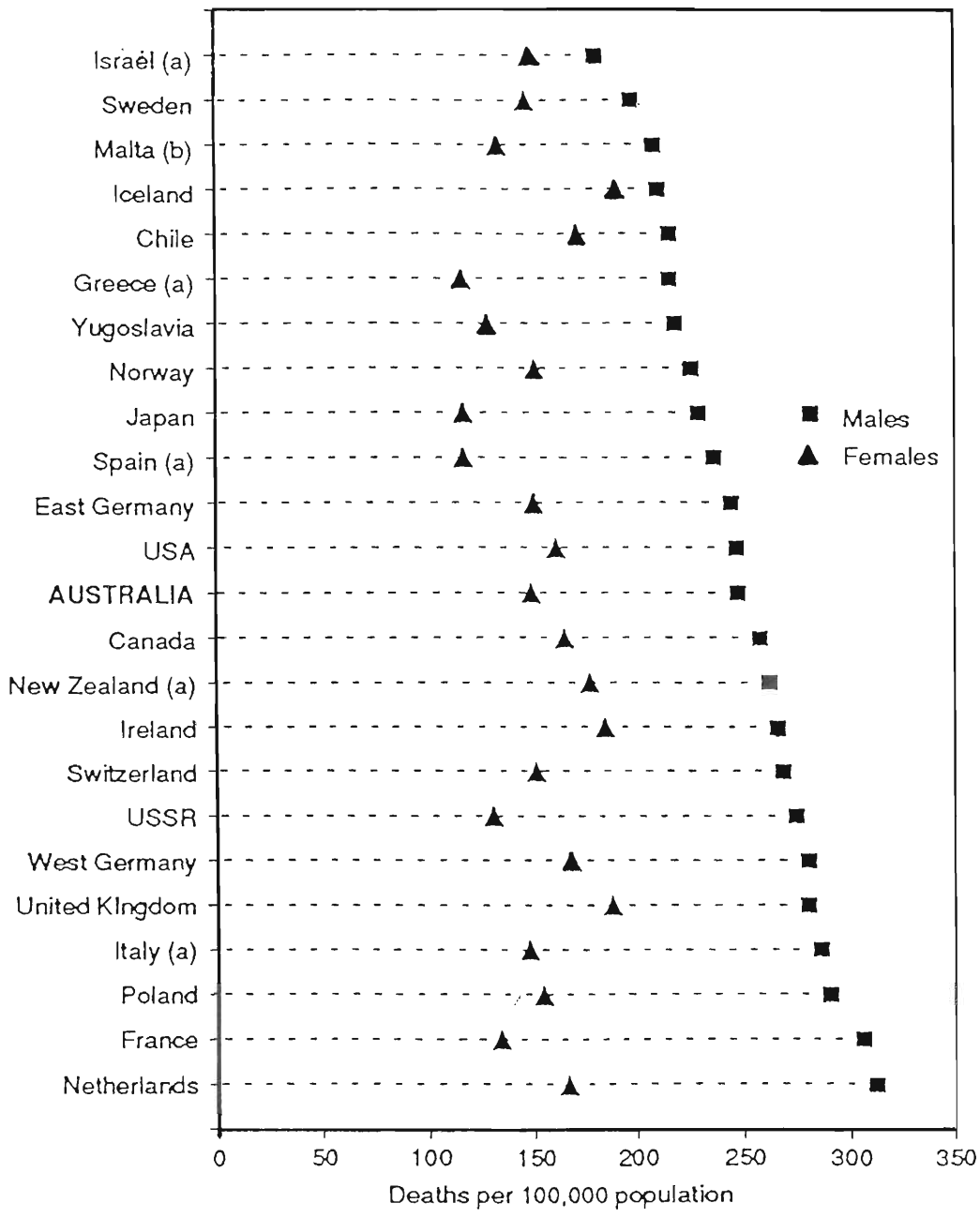
Source: World Health Organization 1988; 1989

FIG. 4 Coronary heart disease deaths, age standardised rates, selected countries, 1987.



Source: World Health Organization 1988

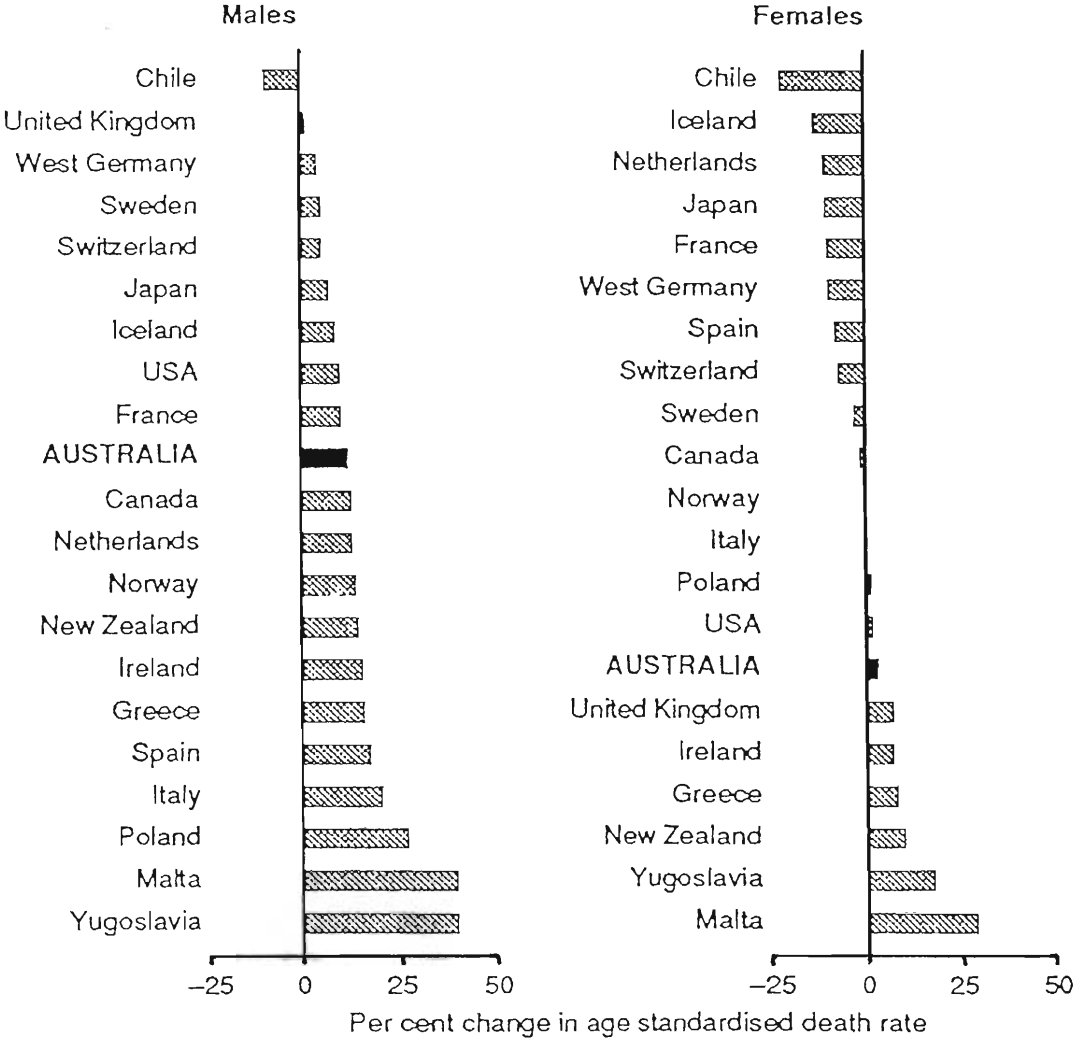
FIG. 5 Coronary heart disease deaths, changes in rates, selected countries, 1965-69 to 1980-84.



(a) Israel, Greece, New Zealand and Italy 1986, Spain 1985
(b) Malta interpolated from 1986 and 1988

Source: World Health Organization 1988; 1989

FIG. 6 Cancer deaths, age standardised rates, selected countries, 1987.



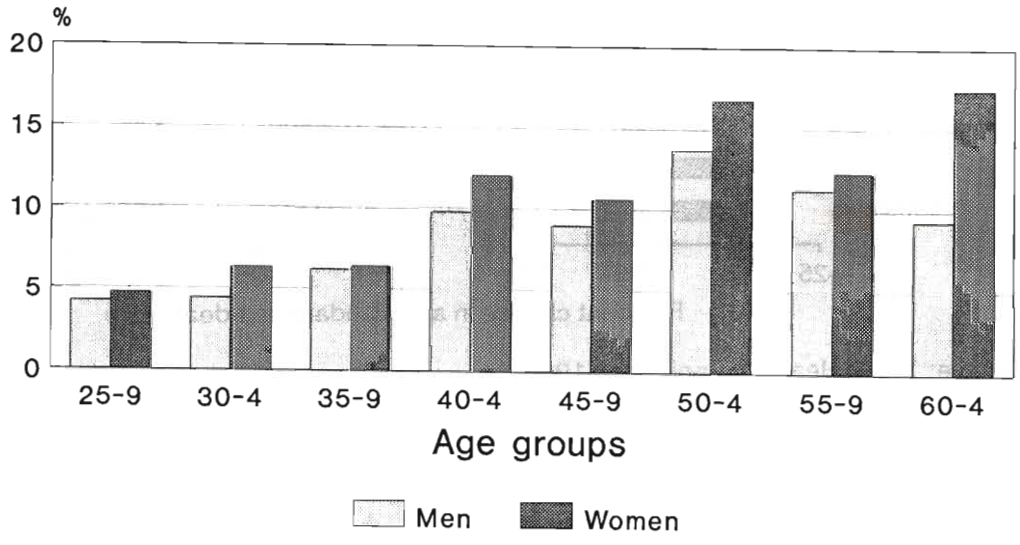
Source: World Health Organization 1988

FIG. 7 Cancer deaths, changes in rates, selected countries, 1965-1969 to980-1984.

over-nutrition we generaly mean positive energy balance, reflected in excessive body fat. Clearly, then, it is possible to have a combination of a nutrient deficiency like that of protein or thiamin and obesity. The problem of obesity continues to worsen in developed countries like Australia (34, 35, 36) (Figures 8a, 8b, 8c). However, there is a growing awareness that the problem of obesity is also on the rise in developing countries, from Asia to Africa. Yet, in developing countries, the combination of under- and over-nutrition is more flagrant since the problems of nutrient deficiencies have not been solved as the problem of positive energy balance has emerged. The basis of this nutritional complexity is, presumably, that, on the one hand, opportunities for physical activity are declining and, on the other hand, the nutritional quality of food is not improving commensurately. If we are less physically active and need to achieve energy balance at a lower plane of energy nutrition, then the nutritional quality of the food we eat must improve (44, 46). The incorporation of more animal fat and refined carbohydrate into the diets of peoples whose level of physical activity is declining is a recipe for obesity.

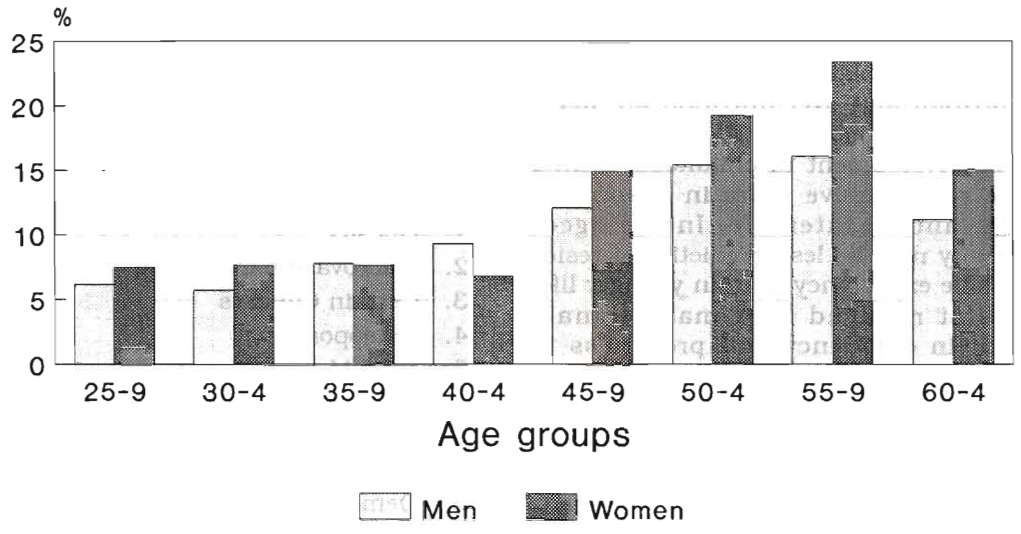
Improved life expectancy in the face of an increasing prevalence of obesity is itself an interesting nutritional situation (Figures 8a, 8b, 8c). That factors other than obesity allow us to cope with it better does not deny the adverse potential of obesity itself. Indeed, to avoid it would presumably be to make even greater health gains. Much more work is needed, nevertheless, to know how much these gains are really possible.

As in other areas of so-called "nutritional status", determinants of body fatness are not always nutritional. This is particularly evident in relation to abdominal fatness, currently appraised by a waist/hip ration (WHR) (10). For example, gender,physical activity itself, cigarette smoking and



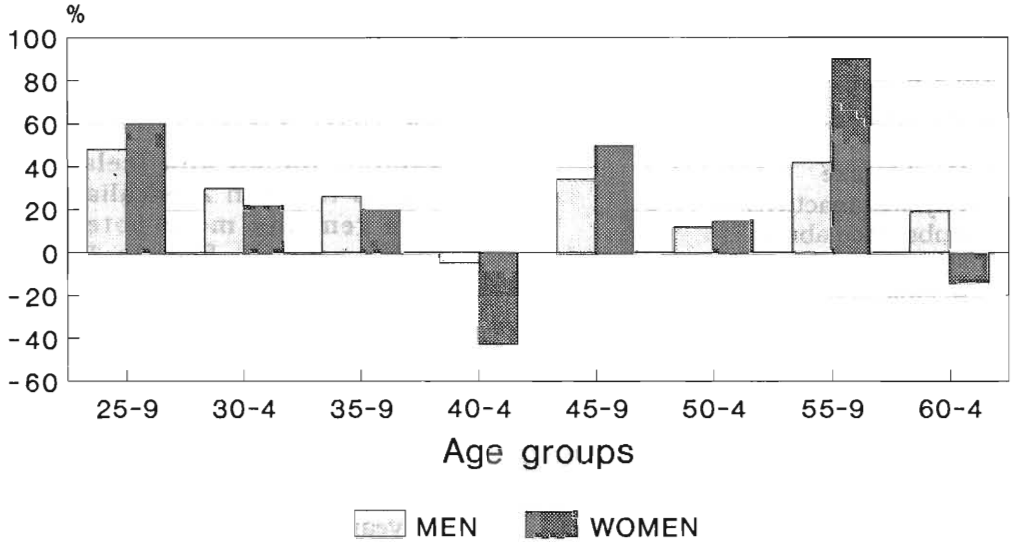
NHF of Australia
Risk Factor Prevalence Survey

FIG. 8a Obesity (BMI-WT/HT^2 > 30) estimates for 1983 men & women.



NHF of Australia
Risk Factor Prevalence Survey

FIG. 8b. Obesity (BMI = $WT/HT^2 > 30$) estimates for 1989 men & women.



NHF of Australia -
Risk Factor Prevalence Surveys

FIG. 8c. Obesity (BMI = WT/HY2 > 30) percentage changes from 1983 to 1989 men & women.

alcohol can all contribute to the distribution of body fat (10).

The problems of combined under-nutrition and over-nutrition are likely to be most consequential during growth and development in childhood, during the reproductive years in a woman's life, and in later life. In the aged, obesity may be less predictive of residual life expectancy than in younger life, whilst reduced lean mass signals protein deficiency and proneness to immunodeficiency (6).

Factor interplay

Food intake is predictive of particular health outcomes in its own right (14, 27, 28, 44).

However, the extent to which food intake is adverse will depend on the interplay with key variables such as physical inactivity, substance abuse (in particular alcohol, tobacco, addictive drugs, and prescription medications), along with environmental factors and aging itself (Table 6).

TABLE 6
Factor Interplay

– Food intake
– Physical inactivity
– Substance abuse
– Environmental factors
– Ageing

Non-communicable diseases

Premature death

For much of human history, infectious disease has been the major cause of premature death and, for women, the problems of childbirth. As the problems have become increasingly under control in developed countries, other causes of premature death have emerged as of greater consequence (Table 7) (1).

TABLE 7
Major non-communicable diseases accounting for premature death in developed countries.

	Directional Change
1. Obesity	▲
2. Macrovascular Disease	▼
3. Certain Cancers	▲ ▻ ▼
4. Osteoporosis	▲
5. NIDDM	▲
6. Alcohol-Related	▻
7. Immunodeficiency in the aged	?
8. Dementa	?

A remarkable phenomen this century is that, although most of the improvement in life expectancy has been attributable to decrease in infant mortality in developed countries, there has been a clear increase in life expectancy at age 80, becoming more in evidence from the 1960's onwards. Thus, in Australia, for men, aged 80, in 1960-62 the life expectancy was 5.6 and, for women aged 80, 6.7, by 1988 this was 6.7 for men and 8.4 years for women (1). Life expectancy in, for example, Japan and Iceland, still exceeds those in Australia, so that there remains more potential for improvement yet. Even in Japan and Iceland, premature death is still in evidence and greater gains in life expectancy must be possible. Maximal achievable life-span, however, must be distinguished from life expectancy and it remains unclear what maximal achievable life-span might be, with most regarding it as in the vicinity of 120 years.

Pattern of eating

For most of the human experience, we were hunters and gatherers (13, 46). Provided the food on which we nibble or graze is not rich in animal fat,

it would appear that this pattern of eating is conducive to health or, at least, reduced cardiovascular risk (22).

A pattern of food intake which is low in refined carbohydrate and low in animal fat, low in sodium, high in unrefined carbohydrate and in fish is the one that appears most conducive to long life expectancies and low morbidity rates (Table 8) (33).

More attention needs to be given to description of food intake by way of integrated or comprehensive indices. For example, the mathematical treatment of food variety and its predictive power for health outcomes is highly desirable (29, 48, 50).

Not all of the current dietary guidelines to encourage plant food can necessarily be read at face value. For example, in Australia, a major contributor to increased fruit consumption has been an increased consumption of fruit juice (3, 8, 9). The loss of physicochemical properties of fruit in the production of fruit juice may lead to significantly different metabolic profiles for glucose and insulin (21).

Industrial urbanisation

Urbanisation has brought with it significant changes to the food supply. For food to be available remote from agricultural production, its transport, processing and storage are required. There is a stimulus to a more assured food supply, provided it can be afforded. The food chain can also be more precarious when any link in the chain is broken. Urbanisation can bring with it the possibility of urban gardens, and it has been estimated, that in some parts of the world as much as 25% of fruit and vegetable production can be obtained locally in an urban setting. A degree of affluence

TABLE 8
Pattern of eating and non-communicable disease

Characterised by	Effect of Industrial Urbanisation
• Nutrient	
▲ Saturated Fat	▲▼
▼ Unrefined Carbohydrate	▲▼
▲ Sodium	▲▼
▲ Alcohol	▲▼
• Food	
▼ Fish	◯▲
▼ Fruit (? Juice)	▲▼
• Food Preparation/Technology	
▲ Fried	▲▼
▲ Extruded	▲▼
? Reassembled	?
? Simulated	?
• Meal/Snack Pattern	
▲ Fatty	▲▼
• Elimination of Seasonal Variation	▲▼

and of major ecological change is, nevertheless, the requisite for this local availability. A sense of loss of control of food supply through less involvement in production and in preparation can be of consequence to food choice. With time, less and less food preparation is taking place in the domestic home and convenience brings with it more and more change in eating habits. The western urban food supply has become characterised by salty and fatty foods from fast-food outlets. A major effort to enable convenience to be part of a healthful food supply is now in evidence in newer food and nutrition policies.

Nutrition-health pathways

An example of how one disease type, macrovascular disease, can arise from several nutritional inputs is shown in "Pathways to Macrovascular Disease" (37, 44, 46) (Figure 9). This same concept applies to other disease entities such as diabetes, osteoporosis and various neoplastic diseases (31, 39, 49, 52, 55, 56).

The new communicable diseases

The World's major health problem complex in developing countries remains that of malnutrition and infectious disease.

However, in developed countries, a new nutrition-communicable disease complex may be emerging. With advancing years, and the advent of a chronic disease itself, immune status may deteriorate. The extent to which this is nutritionally preventable or reversible is an important question (6). Some of it would appear to be nutritionally-dependent (Table 9).

New agents or modes of transmission of infection may also give food intake a changed relevance. For example, HIV positive individuals, as the AIDS complex develops, develop significant nutritional problems. Again, there have been concerns that antibiotic resistance may have, in part, emerged because of animal production practices. New food-borne diseases are distinctly possible (23, 53). The greater use of fruit juices has, in Melbourne, Australia, led to an outbreak of Rota virus induced gastrointestinal tract illness. The problems of Listeriosis have been widely canvassed (23, 53). Whether new food technologies, allowing the production of so-called "functional food", "designer foods" and "food analogues" will alter the opportunities for food-borne diseases remain to be seen.

Well-being

As the prospects for long life expectancy improve and excessive morbidity decreases, more and more people have become interested in well-being in itw own right (Table 10). Its assessment requires better measurement than at present available. It may be self-reported or reflected in health-seeking behaviour.

It is worth noting that a sence of well-being is likely to depend on how adequate or available food is. Again, one of the functions of food is to facilitate social activity. The pleasures of food which derive from its presentation are important in their own right. The frequency of food ingestion has ben much discussed in relation to well-being. Most of the evidence in favour of particular mealtimes and breakfast would suggest that the value of these is culturally bound (11, 12).

A major phenomenon in contemporary society has been an appeal to increase nutrient intakes to improve well-being (42).

There is a legitimate interest in the many classes of compounds in food

TABLE 9

Changing face of communicable disease of nutritional relevance

(a) The immunodeficient
- aged
- wasting disease (e.g. neoplastic, chronic inflammatory bowel disease)
- eating disorders
- immunotropic infection (HIV)

(b) Food-borne
- newer food technology
  - Listeria monocytogenes in dairy products
  - Rota virus in fruit juice (Australian outbreak of 1991)
- food irradiation (contamination without spoiling)
- newer cooking techniques
  - Inappropriate microwave cooking

FIG 9. Pathways to macrovascular Disease.

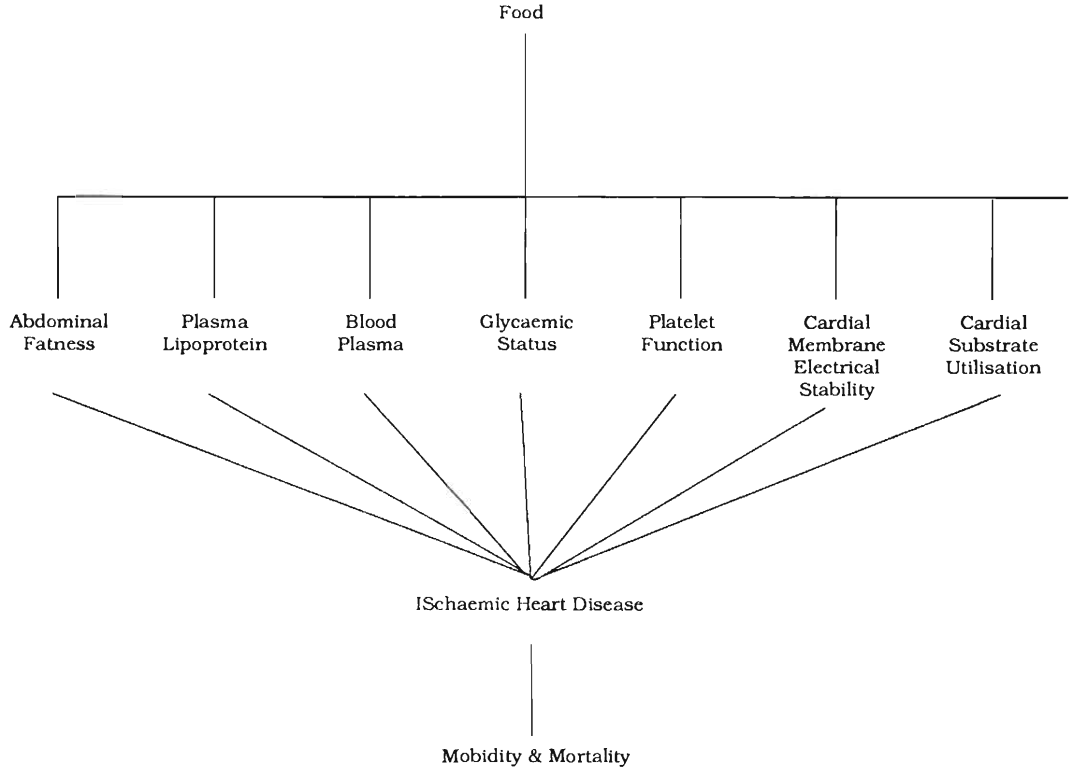


TABLE 10
Well-being

Its measurement
– self-reported
– health-seeking behaviour
Its food dependency
– food supply and availability
– manner of eating (social activity/presentation/frequency)
– nutrient intake
– non-nutrient intake

which may have biological importance,but not be regarded as nutrient. An example of such a class of compounds, phytoestrogens, is of particular relevance to peri-menopausal women (55).

An ecological approach

Ultimately the food chain may be more important for our health than nutrient pathophysiology (Table 11). The need for a sustainable food production with minimal impact on the environment, will increasingly be part of food and nutrition policy. The new "nutrition in transition" will be a re-direction of it with an ecologicl consciousness (45).

TABLE 11

Requirement for an ecological approach to nutrition in transition

– Food production
– Food transport
– Food storage
– Food processing
– Food packaging
– Food preparation
– Food choice

References

1. Australian Institute of Health. Australia's health 1990. The second biennial report of the Australian Institute of Health, Australian Government Publishing Service Canberra; Chapter 2, pp 7-40.
2. Australian Institute of Health. Australia's health 1990. The second biennial report of the Australian Institute of Health, Australian Government Publishing Service Canberra; Chapter 3, pp 41-78.
3. Baghurst K, Crawford D, Record S, Worsley A, Baghurst P, Syrette J. The Victorian Nutrition Survey, Part 1 - Food intakes by age, sex and area of residence. CSIRO Division of Human Nutrition Adelaide 1987.
4. Bastian P. Coronary heart disease in tribal aborigines -the west Kimberley survey. Aust/NZ J Med 1979; 9: 284-292.
5. Birch LL, Johnson SL, Andresen G, Peters JC, Schulte M. The variability of young children's energy intake. New Eng J Med 1991; 324(4): 232-263.
6. Boyce NW, Lukito W, Chandra RK. Nutrition and Immunity. Medical Practice of Preventive Nutrition, Edited by M.L. Wahlqvist and J. Vobecky 1992 (In press).
7. Chong YH, and Pang CW. Serum lipids, blood pressure and body mass index of Orang Asli: Possible effects of evolving dietary and socio-economic changes. Proceedings of the International Workshop on the Effects of Alteration of Food Habits on Health, Osaka, December 1978.
8. Department of Community Services & Health. National dietary survey of adults: 1983 No.1 Foods consumed. Australian Government Publishing Service, Canberra 1986.
9. Department of Community Services & Health. National dietary survey of adults: 1983 No.2 Nutrient intakes.

Australian Government Publishing Service, Canberra 1986.

10. Despres J. Obesity and lipid metabolism: relevance of body fat distribution. Current Opinion in Lipidology 1991.
11. Dickie NH, Bender AE. Breakfast and performance in schoolchildren. Br J Nutr 1982; 48: 483-496.
12. Dunlop W, Wahlqvist ML, Rutishauser IHE, Nestel PJ. The effect of a breakfast-oriented nutrition education program on food intake patterns and alertness of schoolchildren. Proceedings of the Nutrition Society of Australia, VIth Annual Conference, Sydney, New South Wales, Australia, November, 1981. Proc Nutr Soc Aust 1981; 6: 104.
13. Eaton SB, Konner M. Paleolithic Nutrition. A consideration of its nature and current implications. New Eng J Med 1985; 312: 283 - 289.
14. Farchi G, Mariotti S, Menotti A, Seccareccia F, Torsello S, Fidanza F. Diet and 20-year mortality in two rural population groups of middle-aged men in Italy. Am J Clin Nutr 1989; 50: 1095-103.
15. Forbes GB. Children and food - Order amid chaos. New Eng J Med 1991; 324(4): 262-263.
16. Gill T. Potential mediators between social situation and coronary heart disease risk: A Health Promotion Perspective, PhD Thesis, School of Sciences, Deakin University, Geelong, Australia July 1991.
17. Glatthaar C, Welborn TA, Stenhouse NS, Garcia-Webb P. Diabetes and impaired glucose tolerance: A prevalence estimate based on the Busselton 1981 survey. Med J of Australia 143: 436-440.
18. Gleick J. CHAOS: Making a new science. Published in Cardinal by Sphere Books 1988.
19. Hage B and Colleagues. Mark L Wahlqvist Personal communication.
20. Hage BHH, Wahlqvist ML, Oliver RG. Food intake pattern in relation to rice consumption among adult Melbourne Chinese (submitted)
21. Heaton KW, Thornton JR, Emmett PM. Treatment of Crohn's disease with an unrefined-carbohydrate, fibre-rich diet. Br Med J 1979; 2: 764-6.
22. Jenkins DJA, Wolever TMS, Duksan V, Brighenti F, Cunnane SC, *et al.* Nibbling versus gorging: metabolic advantages of increased meal frequency. New Eng J Med 1989; 321: 929-934.
23. Jones D. Foodborne Illness: Foodborne listeriosis. The Lancet 1990; 336: 1171-74.
24. Jurgens H, Peitegen HO, Saupe D. The language of Fractals. Sci Amer August 1990: pp40-47.
25. Kouris A, Wahlqvist ML, Davies L, Scrimshaw NA. Development of a survey instrument for the assessment of food habits and health in later life. In: Proceedings of Congress of Dietitians, Paris, pp 235-239, 1988.
26. Kouris A, Wahlqvist ML, Trichopoulos A, Polychronopoulos E. Food habits and health of elderly in Sparta, Greece: Application of survey instrument. Proceedings XII International Congress on Social and Preventive Medicine, Seoul, 1989, pp 229 - 230.
27. Kushi LH, Lew RA, Stare FJ, Ellison CR, El Lozy M, Bourke G, Daly L, Graham I, Nickey N, Mulcahy R, Kevaney J. Diet and 20-year mortaity from coronay heart disease: The Ireland-Boston Diet-Heart Study. New Eng J Med 1985; 312 (13): 811 - 818.
28. Kromhout D, Bosschieter EB, De

Lezenne Coulander C. Dietary fibre and 10-year mortality from coronary heart disease, cancer and all causes. Lancet 1982; 2: 518-521.

29. Latham D, Bosschieter EB, De Lezenne Coulanders C. The inverse relation betwen fish consumption and 20-year mortality from coronary heart disease. New Eng J Med 1985; 312: 1205-1209.
30. Latham MC, and Scott van Veen M. Dietary guideliness: Proceedings of an International Conference. Toronto, Canada, June 26-27 1988. Cornell International Nutrition Monograph Series, No. 21, 1989.
31. Mann JI. Dietary carbohydrate and metabolic control in diabetes. Diabetes 1988. Proc 13th Congress of the International Diabetes Federation, Sydney, 20-25 Nov 1988. Ed. RG Larkins, PZ Zimmet, DJ Chisholm. Excerpta Medica Amsterdam 1989.
32. McMichael AJ, McCall MG, Hartshorne JM, Woodings TL. Patterns of gastro-intestinal cancer in European migrants to Australia: The role of dietary change. Int J Cancer: 25, 431-437 (1980).
33. National Academy of Sciences, Washington. Recommended Dietary Allowances. Carbohydrates, Fiber and Fat. National Academy Press 1980; 9: 31-38.
34. National Heart Foundation of Australia. Risk factor prevalence study: Report No. 1. National Heart Foundation of Australia and Australian Institute of Health 1980.
35. National Heart Foundation of Australia. Risk factor prevalence study: Report No. 2. National Heart Foundation of Australia and Australian Institute of Health 1985.
36. National Heart Foundation of Australia. Risk factor prevalence study: Report No.3. National Heart Foundation of Australia and Australian Insitute of Health 1989.
37. Nestel PJ. Nutritional control of cardiovascular risk factors. Cardiovascular Risk Factors 1991; 1(5): 259-264.
38. O'Dea K. The hunter-gatherer lifestyle of Australian Abrorigines: implications for health. Current Problems in Nutrition Pharmacology and Toxicology. Publisher John Libbey, London 1988; Chapter 4: 26-35.
39. Partiff AM. Dietary risk factors for age-related bone loss and fractures. Lancet 1983; II: 1181-1184.
40. Powles J. Global patterns and disadvantaged populations. A textbook of Preventive Medicine. Ed. John McNeil, Richard King, Garry Jennings and John Powles. Published by Edward Arnold, Melbourne, Australia 1990.
41. Powles J. Wahlqvist ML, Robbins J, King C. The development of Food and Nutrition Policy in Australia with special attention to the State of Victoria. In: Food and Nutrition Policies, WHO, 1991 (in press).
42. Rutishauser IHE, Wahlqvist ML. Food intake patterns of Greek migrants to Melbourne in relation to duration of stay. Proc Nutrition Society of Australia 1983; 8: 49-55.
43. Truswell S. Evolution of dietary recommended goals and guidelines. Amer J Clin Nutr 1987; 45: 1060-1072.
44. Wahlqvist ML. Nutritional pathways to coronary heart disease: An Overview. Patient Management April 1986; pp 136-143.
45. Wahlqvist ML. Nutritional problems and trend in nutrition research and training in the 90's. In: Pongpaew P, Sastroamidjojo S, Prayurahong P, Migasena P, Rasad A, eds. Human Nutrition Better Nutrition

in Nation Building. Bangkok: Siriyod Printing Co Ltd, 1990; pp 12-22.

46. Wahlqvist ML. International trends in cardiovascular diseases in relation to dietary fat intake: inter-population studies. Diet and Disease; pp 539-543 in Proceedings XIII International Congress of Nutrition, Brighton, UK, August 1985.
47. Wahlqvist ML. The state of nutrition in Australia. In: Williams R, ed. The Science Show. Thomas Nelson Australia, 1983.
48. Wahlqvist ML, Hage B, Powles J, Oliver G, Balazs N. Food variety is protective against cardiovascular risk: A case study of adult Chinese women. The Melbourne Chinese Health Study, 6th Asian Congress Nutriton, Kuala Lumpur, Malaysia, September 16-19, 1991.
49. Wahlqvist ML, Huang S, Worsley A. Use and abuse of vitamins: Food versus pills. The MacMillan Company of Australia Pty Ltd 1987.
50. Wahlqvist ML, Lo CS, Myers KA. Food variety is associated with less macrovascular disease in those with Type II diabetes and their healthy controls. J Amer Coll Nutr 1989; Vol 8, 6: 515-523.
51. Wahlqvist ML, Kouris A, Gracey M, Sullivan H. Rapid assessment procedures and a study of the food habits and health of elderly aboriginal Australians: Junjuwa Community. Proceedings XIII International Congress on Socail and Preventive Medicine, Seoul, 1989, pp 231-232.
52. Wahlqvist ML and Marks S. Diet and Obesity. In: Michael G, ed. Sugars in Nutrition. Norman Kretchmer, Ettore Rossi. Raven Press 1991; pp 179-196.
53. Waites WM, Arbuthnott JP. Food-borne illness: an overview. The Lancet 1990; 336: 721-722.
54. Welborn TA, Glatthaar C, Whittall D Bennett S. An estimate of diabetes prevalence from a national population sample: a male excess. Med J Aust 1989; 150: 78-81.
55. Wilcox G, Wahlqvist ML, Burger HG, Medley G.Oestrogenic effects of plant foods in postmenopausal women. Br Med J 1990; 301: 905-6.
56. Zimmet P, Serjeantson S, Dowse G, Finch C, Collins V. Diabetes mellitus and cardiovascular disease in developing populations: Hunter-gatherers in the Fast Lane. In: Michael G, ed. Sugar in Nutrition. Norman Kretchmer, Ettmore Rossi. Raven Press 1991; 25: 197-212.

Proc 6th ACN 1991: 42-61

Nutrition and immunity: principles and applications

Ranjit Kumar Chandra

Departments of Pediatrics, Medicine, and Bioschemistry, The Gerontology Centre, Memorial University of Newfoundland, and the Division of Immunology, Janeway Child Health Centre, and the World Health Organization Collaborating Centre for Research and Training in Nutritional Immunology, St. John's, Newfoundland, Canada

Introduction

I am honoured to have been asked to give the Plenary Lecture at this prestigious Congress. It is a unique honour and I shall cherish this occasion for a long time. Although I now work in Canada, much of my early work in the field of nutrition and immunity was done in India and my heart is still in Asia.

The theme of my presentation is the barrier that malnutrition and infection create for health and survival. All of you know that infection, often superadded on malnutrition, is a major cause of morbidity in all age groups and is responsible for two-thirds of all deaths under five years of age in developing countries. The prevalence of nutritional deficiencies continues to be high worldwide, and may in fact be increasing in some areas. There are many causes of increased susceptibility to infection among underprivileged malnourished communities, and my talk will focus on impaired immunity as an important contributing factor.

In this selective review, I shall cover four areas :

One, describe our observations on the effects of protein-energy malnutrition and of single nutrient deficiencies on immune responses and risk of infection.

Two, emphasise the importance of nutritional factors in impaired immunity at the two ends of the age spectrum, namely in young infants and in the elderly.

Three, describe the effects of obesity and excessive intake of nutrients on immune responses, and

Finally, give some examples of the practical applications of these observations, and discuss some intervention strategies that can break the shackles created by the conjugate pair of infection and malnutrition.

Early work on malnutrition and immunity

The concept of nutritional deficiency causing impairment of immunocompetence is relatively recent. It is barely 18 years ago when the first systematic studies attempted a comprehensive assessment of immune responses in patients with protein-energy malnutrition (PEM) (1).

The background to our work in this field has been described (2). The severity and extent of dysfunction caused by malnutrition in various organ systems

---

This talk was based on the 1990 McCollum Award Lecture given to the American Society for Clinical Nutrition.

depends on several factors, including the rate of cell proliferation, the amount and rate of protein synthesis and the role of individual nutrients in metabolic pathways. Lymphoid tissues are very vulnerable to this damaging effect. Many cells of the immune system are known to depend for their function on metabolic pathways that employ various nutrients as critical cofactors. Numerous enzymes require the presence of zinc, iron, vitamin B6, and other micronutrients. Any discussion of the effects of nutritional deficiencies on immune responses must be prefaced by emphasising the complexities and heterogeneity of immunocompetent cells, their subpopulations and products such as interleukins and interferons, and other inducer/regulator systems, e.g. complement, involved in immune responses. Also, malnutrition is a complex syndrome where several deficiencies exist simultaneously. Even in laboratory animals deprived of a single nutrient, the functional effects may be the consequence of changes in the absorption or body stores of other substances.

Factors such as lack of health education, illiteracy, poor sanitation, contaminated food and water, and overcrowding are important in leading both to malnutrition and infection. In addition, the consistent impairment of immunity in PEM and the recognised increase in infections in patients with primary immunodeficiencies, is compatible with the hypothesis that depressed immune system in malnutrition enhances the risk and severity of infection.

The immune system

A number of defence mechanisms protect the human host from the entry of microorganisms and development of clinical infection. Host resistance mechanisms can be divided into two main tiers; non-specific and antigen-specific. The non-specific defences include the skin and mucous membranes, phagocytic cells, mucus, cilia, complement, lysozyme, interferon and other humoral factors. These innate processes are naturally present and are not influenced by prior contact with the infectious agent. They act as the first line of protection. Antigen-specific mechanisms include the B cell system of antibody production and the T cell system of cell-mediated immunity. They are adaptive and acquired in that they are specific reactions induced by prior exposure to the microorganism or its antigenic determinants. They are very effective in checking the spread of infection and eradicating the invading organism. More detailed description of the immune system is given elsewhere (3,4).

Field studies

Epidemiological studies have confirmed the causal relationship between malnutrition and infection (5). In the infant illustrated in Figure 1, reduction in two parameters of immunocompetence **preceded** clinical infection and growth faltering. Findings such as these suggest firstly, that altered immune responses at early functional indices of growth failure secondary to latent nutritional deficiency, and secondly, that episodes of infection worsen the child's nutritional state. There was a significant correlation between weight-for-height as an index of protein-energy status and risk of death from infectious disease (6). Morbidity from diarrhoeal disease is increaed (8,9) particularly among those children whose weight-for-height is less than 70 percent of standard (Figure 2). Incidence of diarrhoea is increased slightly but this is not a consistent observation (10). On the other hand, there is a more profound and universally observed effect on duration of each episode. This in turn would be expected to worsen malnutrition (11). Similar observations have

been made with respect to respiratory infection and fever (5,12). In a recent report (13). Victora *et al.* found that malnutrition was a more important risk factor for pneumonia than for diarrhoea whereas diarrhoea was a stronger predictor of malnutrition than was pneumonia, the association being strongest in the first two years of life.

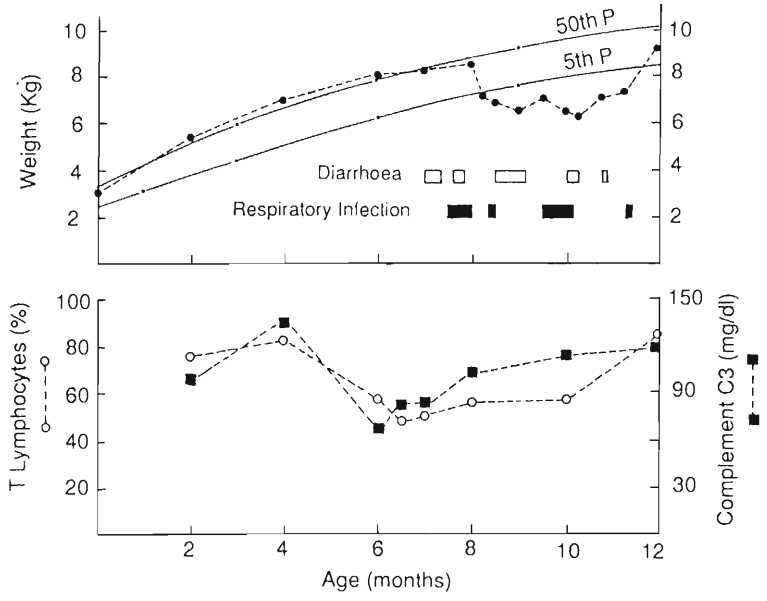


FIG. 1 Course of events in an infant in a village near New Delhi, India, followed from birth until 12 months of age. Soon after weaning at the age of 5 months, there is a reduction in the number of T lymphocyte and the concentration of complement C3 (bottom panel). These immunologic changes precede the occurrence of clinical manifestations (diarrhea, respiratory infection) and the obvious growth faltering seen at about 8 months (upper panel). The findings suggest that immunologic changes are sensitive and functional indices that serve as prognostic indicators of future clinical events.

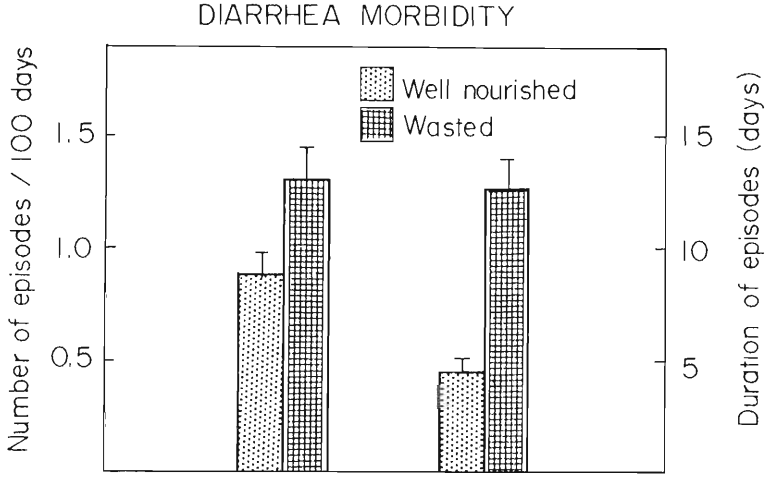


FIG. 2 Differences in morbidity due to diarrhea in well-nourished and wasted (decreased weight-for-height below 70% of NCHS reference standard) infants in rural India.

Pathology of lymphoid tissues

Lymphoid atrophy is a prominent feature of PEM. The thymus was noted to be "a barometer of malnutrition, and a very sensitive one" (14). The term "nutritional thymectomy" illustrates the profound changes that occur in the thymus in malnutrition (12). The size and weight of the thymus are reduced. Histologically, there is a loss of corticomedullary differentiation, there are fewer lymphoid cells, and the Hassal bodies are enlarged, degenerated, and occasionally, calcified. In the spleen, there is a loss of lymphoid cells around small blood vessels. In the lymph node, the thymus-dependent paracortical areas show depletion of lymphocytes.

Immune responses in protein-energy malnutrition

Beisel (15) and Chandra (16) have reviewed the history of early immunologic studies in malnutrition, and several monographs and reviews (6, 12, 17-23) have provided comprehensive listing of work in this field. In PEM, most of the host defence mechanisms are breached (Figure 3). Delayed cutaneous hypersensitivity responses both to recall and new antigens are markedly depressed (Figure 4). It is not uncommon to have complete anergy to a battery of different antigens (1,24). One reason for reduced cell-mediated immunity in PEM is the reduction in mature fully differentiated T lymphocytes that can be recognised by the classical technique of rosette-formation (27, 28) or by the newer method of fluorescent labelling with monoclonal antibodies (29,30). The reduction in serum thymic factor activity observed in primary PEM (31,32) may underlie the impaired maturation of T lymphocytes. There is an increase in the amount of deoxynucleotidyl transferase activity in leukocytes (9), a feature of immaturity. The proportion of helper/inducer T lymphocytes recognised by the presence of CD4+ antigen cell surface is markedly decreased (Figure 5). There is a moderate reduction in the number of suppressor/cytotoxic CD8+ cells. Thus the ratio CD4+/CD8+ is significantly decreased compared with that in well nourished controls (30). Moreover, coculture experiments have shown a reduction in the number of antibody producing cells (29) and in the amount of immunoglobulin secreted. This may largely be due to decreased "help" provided by T lymphocytes (Figure 6). Lymphocyte proliferation and synthesis of DNA are reduced, especially when autologous patient's plasma is used in cell cultures. For example, lymphocytes traffic and homing pattern are also altered (34).

A review of the literature (5, 6, 12, 29-22) suggests that serum antibody responses are generally intact in PEM, particularly when antigens in adjuvant are administered or in the case of those materials that do not evoke T cell response. There are rare exceptions, such as Salmonella typhi. One must carefully rule out infection as a confounding factor. Recently, we have found that antibody affinity is decreased in patients who are malnourished (36). This may provide an explanation for a higher frequency of antigen-antibody complexes found in such patients (18). Secretory IgA antibody levels after deliberate immunisation with viral vaccines are decreased (37); there is a selective reduction in secretory IgA levels (38). This may have several clinical implications, including an increased frequency of septicemia commonly observed in undernourished children.

Phagocytosis is also affected in PEM. The level and activity of most complement components are decreased (39-41). The best documented is a reduction in complement C3, C5, factor B, and total haemolytic activity. The ingestion of particles by phagocytes is intact, but their subsequent metabolic

FIG. 3 A simple view of host defenses as a protective umbrella. It consists of physical barriers (skin, mucous membranes), non-specific mechanisms (complement, interferon, lysozyme, phagocyte), and antigen-specific processes (antibodies of five immunoglobulin isotypes and cell-lediated immunity. In protein-energy malnutrition, most of the host defense mechanisms are breached, allowing microbus to invade and produce clinical infection which is more severe and prolonged. Copyright ARTS Biomedical Publishers 1981.

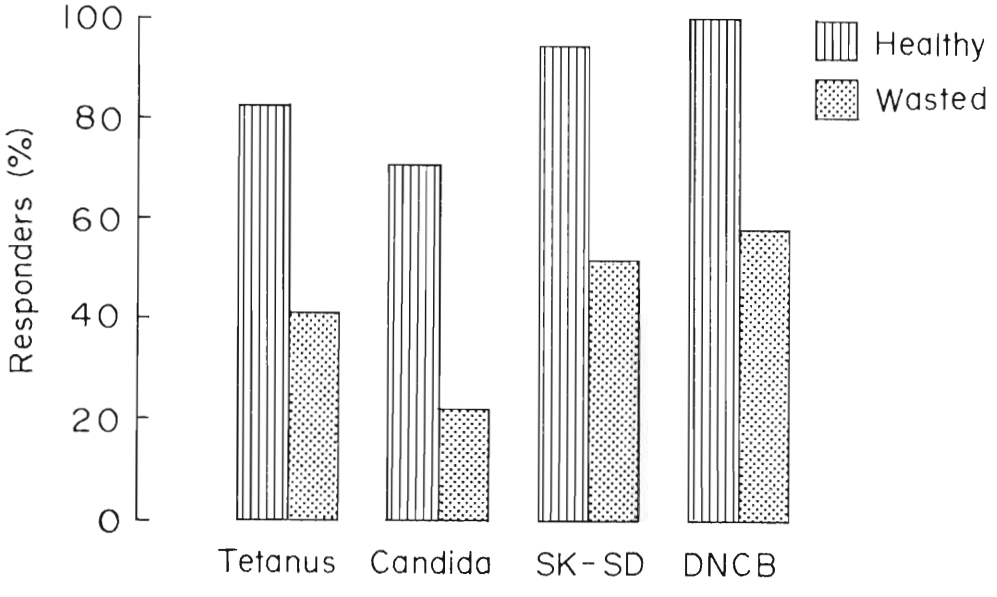


FIG. 4 Delayed hypersensitivity skin responses. The percentage of young children who showed a positive response to various antigens is shown. SK-SD, streptokinase-streptodornase; DNCB, 2,4-dintrochlorobenzene. There is marked reduction in the proportion of wasted children who respond to these recall antigens and chemical sensitization.

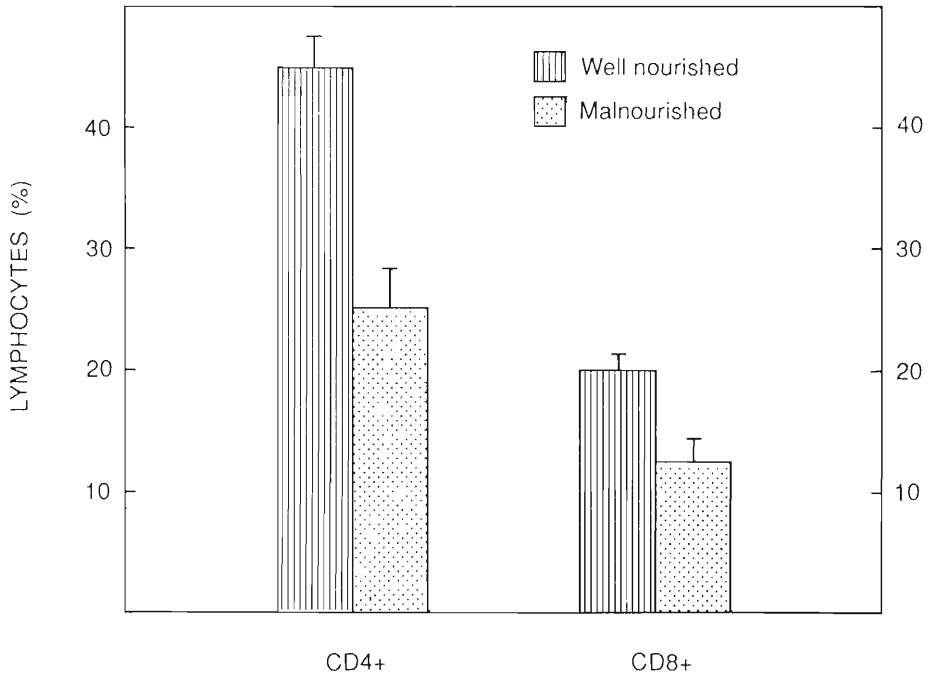


FIG. 5 The proportion of two subsets of T lymphocytes in well-nourished and malnourished children.

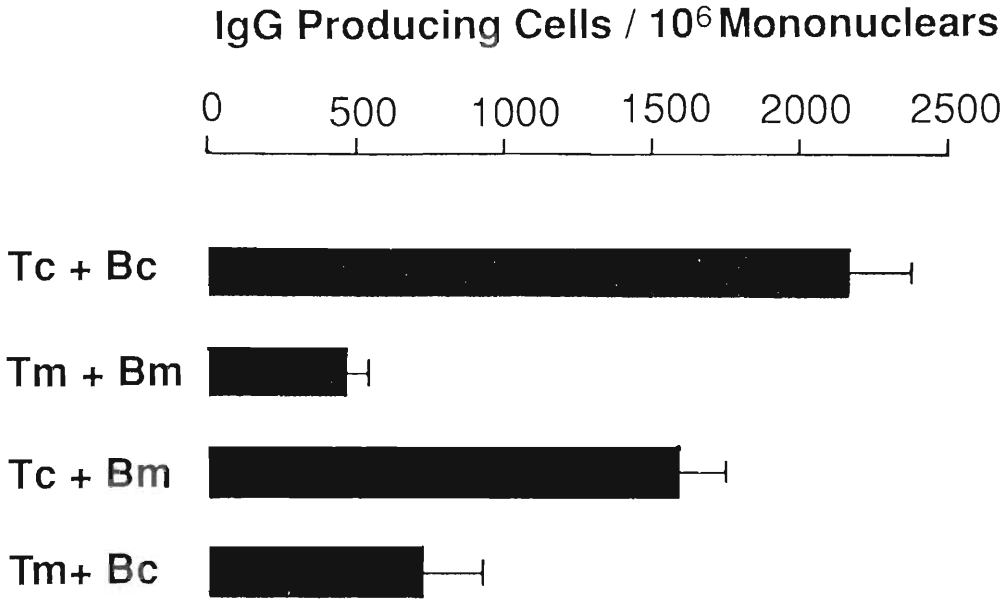


FIG. 6 Immunoglobulin production in co-culture experiments where T and B lymphocytes are mixed and are stimulated with poke weed mitogen for seven days. Ig G producing cells are recognized by lyric areas in a reverse hemolytic plaque assay. Compared with well nourished controls (first column), there is a marked reduction in the number of antibody producing cells in malnourished children (second column). When T cells of healthy controls (Tc) are mixed with B cells of malnourished patients (Bm), there is a significant improvement in response (third column), whereas the opposite combination (Tm + Bc) results in a moderate increase (fourth column).

activation and destruction of bacteria is reduced. Finally, recent work in man and animals had demonstrated that the production of several cytokines including interleukins 1 and 2 and gama-interferon is decreased in PEM. Moreover, malnutrition alters the ability of T lymphocytes to respond appropriately to cytokines (42).

There is very little work on the effect of malnutrition on the integrity of physical barriers, quality of mucus or several other innate immune defences. For examples, quality of mucus or several other innate immune defences. For example, lysozyme levels are decreased (43) and adherence of bacteria to epithelilal cells is increased in PEM (44).

Micronutrient deficiencies and immune responses

The topic of micronutrients and immune functions has been reviewed extensively (45-50). This recent interest has been prompted by a number of observations that indicate the crucial role of several nutrients in key metabolic pathways and cell functions. Isolated deficiencies of micronutrients are rare with the exception of iron, vitamin A and zinc. However, human malnutrition is usually a composite syndrome of multiple nutrient deficiencies. Observations in laboratory animals deprived of one dietary element and findings in the rare patient with a single nutrient deficiency have confirmed the crucial role of several vitamins and trace elements in immunocompetence.

Four general concepts have been advanced (51): **One**, alterations in immune responses occur early in the course of reduction in micronutrient intake. **Two**, the extent of immunologic impairment depends upon the type of nutrient involved, its interactions with other essential nutrients, severity of deficiency, presence of concomitant infection, and age of the subject. **Three**, immunologic abnormalities predict outcome, particularly the risk of infection and mortality. **Four**, tests of immunocompetence are useful in titration of physiologic needs and in assessment of safe lower and upper limits of intake of micronutrients.

Vitamin A deficiency results in decreased lymphocyte proliferation in responses to mitogens, antigen-specific antibody production and T lymphocyte proliferation *in vitro*, and increased bacterial adherence to respiratory epithelial cells (52-55). Vitamin A deficiency is believed to impact both on morbidity and mortality (56) but the precise quantitative relationships for these interactions have to be worked out. Carotenoids have important immunoregulatory functions involving T and B lymphocytes, natural killer cells and macrophages. Vitamin B6 deficiency causes profound changes in immune responses in animals (57-59) including cell-mediated immunity and antibody formation. Moderately severe deficiency of vitamin C is associated with retarded locomotion and decreased bactericidal capacity of neutrophils and macrophages; cell-mediated immunity and antibody production are relatively unaffected (6). Severe vitamin E deficiency results in impaired cell-mediated immunity and decreased antibody synthesis.

Zinc deficiency, both acquired and inherited, is associated with lymphoid atrophy, decreased cutaneous delayed hypersensitivity responses and homograft rejection, and lower thymic hormone activity (61-65). This is best illustrated in patients with acrodermatitis enteropathica (Table 1) who have impaired lymphocyte response to phytohemagglutinin, decreased thymulin activity and reduced delayed hypersensitivity skin reactions (66). In laboratory animal models one can demonstrate reduced number of antibody-forming cells in the spleen and impaired T-killer cell activity (62).

impaired T-killer cell activity (62). There is decreased ingestion and phagocytosis. The nutrient is probably involved in stimulation of NADPH oxidase through its role as a cofactor for phospholipase A2 and/or phospholipase C. Zinc may stabilise 20:4 arachidonic acid against oxidation by iron complexes. Zinc complexes may react with oxygen, generating products highly toxic to ingested pathogens. Wound healing is impaired. Zinc deficiency promotes infestation of nematodes (67). Copper deficiency may occur rarely in association with PEM and results in altered immune responses (68). These changes are organ-specific and are influenced by the type of carbohydrate in the diet (69). The function of reticuloendothelial system is depressed and the mircobicidal activity of phagocytes is decreased. This has been attributed to the role of copper in superoxide dismutase and cytochrome c oxidase enzyme systems. There is a reduction in antibody response to T cell dependent antigens.

Deficiency of iron is the commonest nutritional problem worldwide, even in industrialised countries. On the one hand, free iron is necessaray for bacterial growth: removal of iron with the help of lactoferrin or other chelating agenst reduced bacterial multiplication, particularly in the presence of specific antibody. On the other hand, iron is needed by natural killer cells, neutrophils and lymphocytes (Figure 7) for optimal function. Thus, bactericidal capacity is reduced in iron deficiency. Does the amount of dietary iron influence the risk of infection? (70,71). The concept of "iron nutritional immunity" emphasising the effect of iron deprivation in limiting the multiplication of bacteria is an attractive hypothesis with considerable *in vitro* evidence but clinical data do not support the suggestion that iron deficiency protects against infection or that correction of iron deficiency particularly if it is achieved gradually by oral iron therapy increases the incidence or severity of infectious disease in man.

The role of other micronutrients and of toxic heavy metals has been reviewed elsewhere (45-50, 72-74).

Amino acids modulate immune responses in many different ways (75-77). There is recent evidence for the

TABLE 1
Immunological findings in acrodermatitis enteropathica

Parameter	Before therapy	After therapy
Number of patients	8	8
Serum zinc (μg/l) Mean ± SE	48.4 ± 11.3	89.0 ± 8.7
Delayed hypersensitivity skin reactions (No. positive/tested)	3/8	8/8
Serum thymulin (median)	1:2	1:32
Lymphocyte response to phytohemagglutinin Mean ± SE	23.4 ± 17.6	79.5 ± 12.4

Patients were treated with oral zinc 150 mg daily for 6 weeks

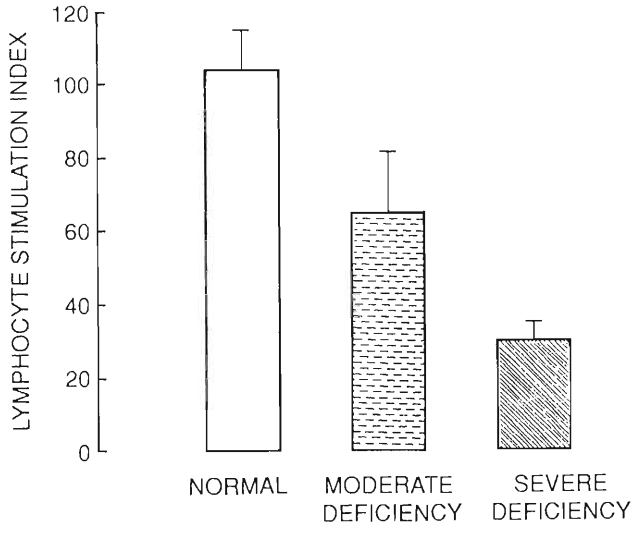


FIG. 7 Lymphocyte stimulation index in moderate (ferritin 12-30 ng/ml, normal hemoglobin concentration) and severe (ferritin <12 ng/ml, anemia) iron deficiency. Cells were cultured in e presence of phytohemagglutinin.

role of glutamine and arginine (78,79).

There is much evidence to indicate that dietary lipids have an immunoregulatory role (80-86). The postulated pathogenetic mechanisms include modulation of eicosanoid synthesis, changes in cell membrane, altered number and density of receptors, changes in the number and function of selected subsets of cells, and altered production and action of cytokines. Essential fatty acid deficiency reduces a variety of immune responses.

Immunocompetence of low birth weight infants

Neonates have suboptimal immune responsses and are susceptible to infection. When growth retardation and nutritional deficiency complicate the picture, as in low birth weight infants, impairment of immunocompetence is more marked and longer-lasting (87-93).

Small-for-gestational age infants show prolonged impairment of cellular immunity (Figure 8). Serum thymic factor is low (91). In contrast to AGA low birth weight infants who recover immunologically by about 2-3 months of age, SGA infants continue to exhibit impaired cell-mediated immune responses for several months or even years (89). This is particularly true of those infants whose weight-for-height is less than 80% of standard. The prolonged immunosuppression in some SGA infants correlates with clinical experience of infectious illness (92), and thus may have considerable biological significance. In animal models of intrauterine nutritional deficiency, PEM (Figure 9) (94) as well as deprivation of selected nutrients (95,96) results in reduced immune responses in the offsping (Figure 10).

Phagocyte function is deranged and physiological hypoimmunoglobulinaemia G is pronounced and prolonged in LBW infants (87). There is a progressive rise in IgG concentration with gestational age and birth weight, especially in infants below 2,500 g (90). All four subclasses of IgG are detected in foetal sera as early as 16 weeks of gestation, the bulk being formed by IgG1. In SGA LBW infants, the cord

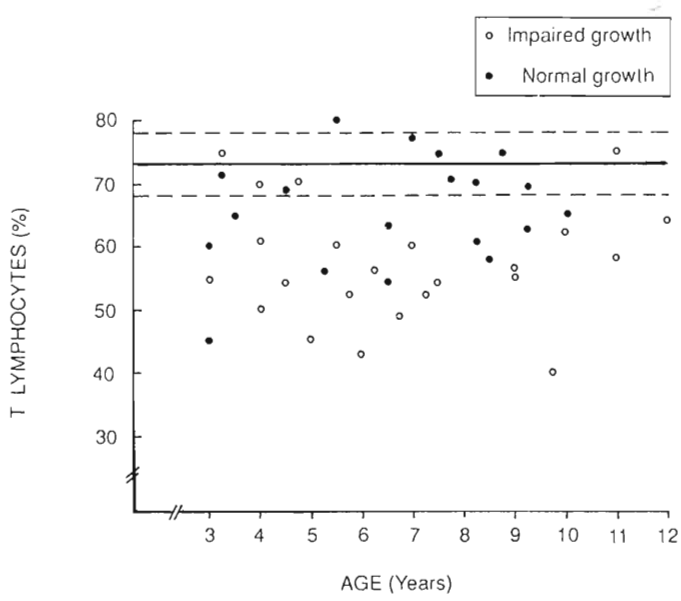
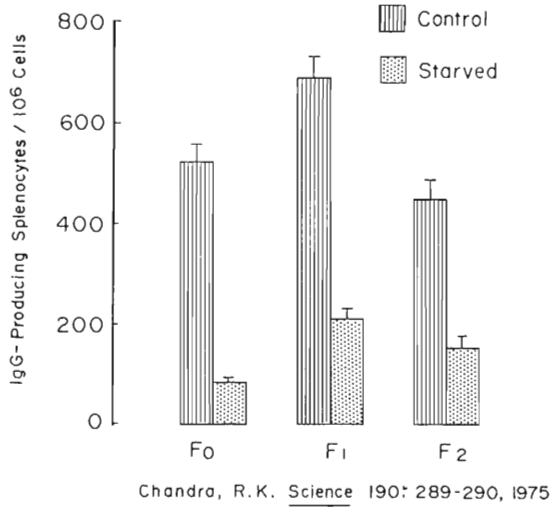


FIG. 8 Number of T lymphocytes in small-for-gestation low birth infants seen at various ages from 3 to 12 years. The mean and 95% confidence limits of normal values are shown as the continuous and interrupted lines respectively. Children who had caught up in anthropometic measurements (o) Showed near-normal or slightly reduced number of T cells, whereas those children who continued to have low weight-for-height (o) generally showed a significant reduction in the number of T lymphocytes.

FIG. 9 Intergenerational effects of nutritional deficiency, IgG-antibody producing spleen cells were estimated in mice subjected to partial starvation (65% of energy intake in controls). The offspring were given *ad libitum* access to food. The F1 and F2 generation offspring of starved female dams mated with healthy well nourished males showed a significant reduction min antibody response. F0 and F1 animals were tested at age 9 weeks and F2 at age 6 weeks. Copyright American Association for Advancement of Science 1975.



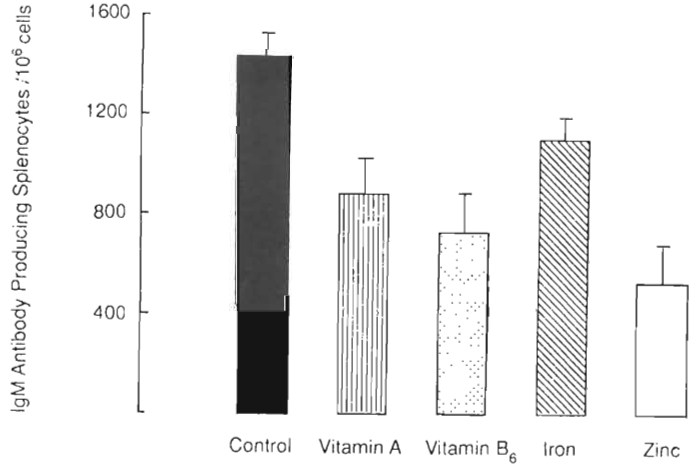


FIG. 10 The effect of selected single nutrient deficiencies before and during gestation on IgM antibody production in the offspring. The rank order of the magnitude of effect was zinc, vitamin B6, vitamin A and iron. The design of the experiment was similar to that in Fig. 9, execpt only F1 generation offspring were tested.

blood levels of IgG1 are reduced much more than those of other subclasses. Thus the infant : maternal ratio is significantly low for IgG1 but not for IgG2. The number of immunoglobulin-producing cells and the amount of immunologlobulin secreted is decreased in SGA infants who are symptomatic, i.e. those who have recurrent infections (92). In the second year of life, SGA infants show a marked reduction in IgG2 levels and often show infections with organisms that have a polysaccharide capsule.

In preterm infants with birth weight between 1800 and 2200 g, moderate amounts of oral zinc supplements accelerate immunologic recovery (Table 2).

immune responses. **Four**, if nutritional therapy improves immunity, will this result in reduced illness.

A critical review of published work related to nutrition, immunity and morbidity in old age has been presented (98). It has been observed that **average** of immune responses in the elderly is significantly lower than that seen in the young. However, there is a much wider range of responses found in the former, so that there are some among the very old whose immune responses are as vigorous as those observed in younger subjects. Several surveys have shown that almost one-third of apparently healthy elderly have reduction in the intake of several nutrients; this is reflected to

TABLE 2
Zinc supplementation of pre-term low birth weight infants

Parameter	Supplemented	Control
Number	18	16
T lymphocytes (%)	56 ± 4	38 ± 6
Lymphocyte response to phytohemagglutin	62 ± 12	21 ± 7
Serum thymulin activity (Median)	1:32	1:8

Infants received oral zinc 1 mg/kg body weight daily. The infants were tested at age 4 weeks.

Nutritional and immunity in old age

Four questions have been posed (98). **One**, is immunologic decline an inevitable part of aging? **Two**, how common are nutritional deficiencies in the elderly. **Three**, would correction of nutritional deficiencies improve some extent in reduced blood concentrations. The most common deficiencies are those of iron, zinc, and vitamin C. Correction of these deficiencies by nutritional advice, dietary or medicinal supplements results in a significant improvement in immunocompetence. There is recent evidence to indicate

that improved immune responses are associated with decreased morbidity due to common respiratory infections.

Immune responses in obesity and excessive intake of nutrients

Genetically obese animals show alterations in a variety of immune responses (99). Natural killer cell activity is decreased. The generation of cytotoxic T lymphocytes following stimulation *in vivo* is decreased but is normal if sensitisation is carried out *in vitro*. This suggests that the microenvironment of the obese animal, including hyperlipidemia, hyperglycemia and altered levels of insulin, glucagon, cortisol and adrenocorticotrophic hormones, may be responsible for impaired cellular responses. Obese adolescents and adults show a higher risk of infection, including post-operative sepsis than lean controls (100). In the obese, there is a slight impairment of delayed cutaneous hypersensitivity responses, decreased lymphocyte response to mitogens, and reduced bactericidal capacity of neutrophils (101).

Recent work has confirmed that excess lipid intake impairs immune responses (102-105). An increase in either saturated fat or polyunsaturated fatty acids to more than 16% of calories results in decreased cell-mediated immunity including cytotoxic function, delayed cutaneous hypersensitivity, lymphocyte response to mitogen stimulation, and natural killer cell activity. In autoimmune diseasse prone mice, reduction in fat intake protects against immune complex pathology (106).

A slight excess intake of certain nutrients may be associated with enhanced immune responses. These include beta-carotene, vitamin A, vitamin E, zinc and selenium. Increased amounts of selected amino acids, such as arginine (79), and other compounds such as nucleotides (107) are reported to enhance immune responses, particularly in the face of stress such as burns, trauma or sepsis (78). It must be emphasised that all nutrients given in quantities beyond a certain threshold will reduce immune responses. This has been shown for zinc (108), selenium, and vitamin A (Fig. 20) and vitamin E. Iron overload may promote bacterial septicemia and increase the frequency of symptomatic malaria in endemic areas.

Applied significance

Nutritional regulation of immunity and risk of illness have several practical applications. Firstly, changes in immune responses occur early in the course of nutritional deficiency. Thus, we can employ immunocompetence as a sensitive functional indicator of nutritional status. In patients with obvious primary or secondary malnutrition, the number of T lymphocytes is a useful measure of response to supplementation therapy. Secondly, anergy and other immunological changes correlate with poor outcome both in medical and surgical patients in terms of complications, duration of hospital stay and mortallity. This is particularly useful when impaired immunity is considered in association with hypoalbuminemia (4,109). In field surveys, impaired cell-mediated immunity and reduced levels of complement components precede and predict the occurrence of infection (Figure 1). Thirdly, opportunistic infections occur more frequently among those patients with cancer who are also malnourished. The incidence of complicating infections can be reduced if appropriate preventative and therapeutic nutritional management is carried out in patients with leukemia. Fourthly, there is an uncanny similarity between the immunologic findings in nutritional deficiencies and those seen in AIDS (110,111). It has been postulated that nutritional deficiency may influence the biologic gradient and natural history of this infection. Recent

surveys indicate that attention to the nutritional needs of the HIV-infected individual is an important part of the overall management of this life-threatening infection (112). Fifthly, response to immunisation is modulated by the nutritional status of the host and protective efficacy of vaccines may be suboptimal in the undernourished individual (113). Finally, immune responses can be used to define safe upper and lower limits of nutrients intake.

Intervention strategies

I shall now outline some intervention strategies that can reduce the incidence and adverse health impact both of malnutrition and infection, with emphasis on young children. We already have much of the knowledge needed to improve health rapidly; what is lacking is political commitment and effective management. Even within the health sector, there are glaring anomalies. We must assign priorities (114) and implement methods to prevent and control contributors to morbidity and mortality.

Improvement in socio-economic status and education and ensuring availability of sufficient food will eliminate much of malnutrition and infection, the disease of poverty. Health and self-limitation of family size will usually follow these measures. Promotion of breast-feeding should be continued. The anti-infective properties of human milk are well known and depend in part upon various cellular and soluble factors, as well as its buffering capacity and several antigen-nonspecific protective factors (115). The benefit is most dramatic in underprivileged communities with poor sanitation, inadequate housing and contaminated food and water (116-118). Furthermore, breast-feeding contributes to birth spacing, an important factor in both maternal and child health.

More effective immunisation programmes against the common communicable diseases are required for the majority of the susceptible population. There is serious concern over the number of children in developing countries who die or are disabled from preventable infectious diseases. Immunisation programmes should include universal coverage of all the population at risk. In addition, there is need to develop new vaccines such as those for malaria, shigella and Pneumococcus, and improve the quality of those against typhoid, cholera and tuberculosis. In addition, new methods of vaccine preparation, such as genetic recombination, subunit antigens, synthetic peptide antigens, anti-idiotypes, and host cell receptor specific vaccines show great promise. It would be ideal to have a single efficacious inexpensive vaccine containing immunising antigens for several infections, be given at birth, be easy to administer, be stable on exposure to light and tropical temperatures, and have no serious adverse effects. Other useful preventative measures include availability of plentiful clean water, improved sanitation and housing, early and adequate management of diarrhoea and respiratory infections using oral rehydration solution and antibiotics respectively, detection of growth faltering using simple growth charts, and sometime, targeted subsidies and massive campaigns to eliminate specific nutrient deficiencies such as those of vitamin A, iron and iodine.

Concluding remarks

In summary, malnutrition and infection are the two major shackles to development and survival, and poverty and ignorance are the most significant contributing factors. Our greatest gift to the new millennium will be to reduce illness and debility in all age groups. The issue is particularly important and immediate for children, because the

child cannot wait until tomorrow,
which may never dawn for him.

"We are guilty of many errors and many faults,
but our worst crime is abandoning the children,
neglecting the fountain of life.
Many of the things we need can wait. The child cannot.
Right now is the time his bones are being formed;
his blood is being made and his senses are being developed.
To him we cannot answer - "Tomorrow."
His name is "Today."

Gabriela Mistral

References

1. Chandra RK. Immunocompetence in undernutrition. J Pediatr 1972; 81: 1194-1200.
2. This week's Citation Classic. Current Contents 1987; 30:15.
3. Roitt IM, Brostoff J. Immunology. London: Gower, 1985.
4. Chandra RK, ed. Primary and secondary immunodeficiency disorders. Edinburgh; Churchill Livingstone, 1983.
5. Scrimshaw NS, Taylor CE, Gordon JE. Interactions of nutrition and infection. Geneva, World Health Organization, 1968.
6. Chandra RK. Nutrition, immunity and infection. Present knowledge and future directions. Lancet 1983; i:688-691.
7. Purtilo DT, Connor DH. Fatal infections in protein-calorie malnourished children with thymolymphatic atrophy. Arch Dis Child 1975; 50:149-152.
8. Tomkins A. Nutritional status and severity of diarrhoea among preschool children in rural Nigeria. Lancet 1981; i:860-862.
9. Chandra RK. The nutrition-immunity-infection nexis: the enumeration and functional assessment of lymphocyte subsets in nutritional deficiency. Nutr Res 1983; 3:605-615.
10. James JW. Longitudinal study of the morbidity of diarrheal and respiratory infections in malnourished children. Am J Clin Nutr 1972; 25:690-94.
11. Martorell R, Yarbrough C. The energy cost of diarrheal diseases and other common diseases in children. In: Chen L, Scrimshaw NS, eds. Diarrhoea and malnutrition. Interactions, mechansisms and interventions. New York: Plenum Press, 1983; 125-41.
12. Chandra RK, Newberne PM. Nutrition, immunity and infection. Mechanisms of interactions. New York: Plenum, 1977.
13. Victora CG, Barros FC, Kirkwood BR, Vaughan JP. Pneumonia, diarhoea, and growth in the first 4 y of life: a longitudinal study of 5914 urban Branzialian children. Am J Clin Nutr 1990; 52:391-6.
14. Simon J. A physiological essay on the thymus gland. London: Renshaw, 1845; 1-100.
15 Beisel WR. The history of nutritional immunology. J Nutr Immunol 1991 (in press).

16. Chandra RK. Immunocompetence in protein-energy malnutrition, a historical perspective. J Nutr 1991 (in press).

17. Suskind R, ed. Malnutrition and the immune response. New York: Raven Press, 1977.

18. Chandra RK. Immunology of nutritional disorders. London: Edward Arnold, 1980.

19. Keusch GT, Wilson CS, Waksal SD. Nutrition, host defences, and the lymphoid system. Arch Host Def Mech 1983; 2:275-359.

20. Gershwin ME, Beach RS, Hurley LS. Nutrition and immunity. New York: Academic Press, 1984.

21. Watson RR, ed. Nutrition, disease resistance, and immune function. New York: Marcel Dekker, 1984.

22. Chandra S, Chandra RK. Nutrition, immune responses, and outcome. Prog Food Nutr Sc 1986; 10:1-65.

23. Chandra RK, ed. Nutrition and immunology. New York: Alan R. Liss, 1988.

24. Smythe PM, Brerton-Stiles GG, Grace HJ, *et al.* Thymolymphatic deficiency and depression of cell-mediated immunity in protein-calorie malnutrition. Lancet 1971; ii:939-43.

25. McMurray DN, Loomis SA, Casazza LJ, Rey H, Miranda R. Development of impaired cell-mediated immunity in mild and moderate malnutrition. Am J Clin Nutr 1981; 34:68-77.

26. Kielmann AA, Uberoi IS, Chandra RK, Mehra VL. The effect of nutrition status on immune capacity and immune responses in preschool children in a rural community in India. Bull Wld Hlth Org 1976; 54:477-483.

27. Chandra RK. Rosette-forming T lymphocytes and cell-mediated immunity in malnutrition. Br Med J 1974; 3:608-609.

28. Bang BG, Mahalanabis D, Mukherjee KL, Bang FB. T and B lymphocyte rosetting in undernourished children. Proc Soc Exp Biol Med 1975; 149:199-201.

29. Chandran RK. Numerical and functional deficiency in T helper cells in protein-energy malnutrition. Clin Exp Immunol 1983; 51:1216-132.

30. Chandra Rk, Gupta S, Singh H. Inducer and suppressor T cell subsets in protein-energy malnutrition. Analysis by monoclonal antibodies. Nutr Res 1982; 2:21-26.

31. Chandra RK. Serum thymic hormone activity in protein-energy malnutrition. Clin exp Immunol 1979; 38:228-230.

32. Wade S, Bleiberg FK, Moose A, *et al.* Thymulin (Zn-Facteur thymique serique) activity in anorexia nervosa patients. Am J Clin Nutr 1985; 41:275-280.

33. Beatty DW, Dowdle EB. The effects of kwashiorkor serum on lymphocyte transformation *in vitro*. Clin Exp Immunol 1978; 32:134-143.

34. Chandra RK. Nutritional regulation of immunity and infection. From epidemiology to phenomenology to clinical practice. Golan Memorial Lecture . J Pediat Gast Nutr 1986; 5:844-852.

35. Reddy V, Srikantia SG. Antibody response in kwashiorkor. Ind J Med Res 1964; 52:1154-1158.

36. Chandra RK, Chandra S, Gupta S. Antibody affinity and immune complexes after immunization with tetanus toxoid in protein-energy malnutrition. Am J Clin Nutr 1984; 40:131-134.

37. Chandra RK. Reduced secretory antibody response to live attenuated measles and poliovirus vaccines in malnourished children. Br Med J 1975; 2:583-585.

38. Watson RR, McMurray DN, Martin P, Reyes MA. Effect of age, malnutrition and renutrition on free secretory components and IgA in secretions. Am J Clin Nutr 1985; 41:281-288.

39 Chandra RK. Serum complemet and immunoconglutinin in malnutrition. Arch Dis Child 1975; 50:225-229.

40. Srisinha S, Edelman R, Suskind R, *et al.* Complement and C3 proactivator levels in children with protein-energy malnutrition and effect of dietary treatment. Lancet 1975; i:1016.

41. Haller L, Zubler RH, Lamber PH. Plasma levels of complement components and complement hemolytic activity in protein-energy malnutrition. Clin exp Immunol 1978; 34:248-254.

42. Hoffman-Goetz L, Bell RC, Deir R. Effect of protein malnutrition and interleukin-1 on *in vitro* rabbit lymphocyte mitogenesis. Nutr Res 1984; 4:769-780.

43. Chandra RK, Chandra S, Khalil N, Howse D, Kutty KM. Lysozyme (muramidase) activity in plasma, neutrophils and urine in malnutrition and infection. In: Suskind RM, ed. Malnutrition and the immune response. New York: Raven Press, 1977; 407-9.

44. Chandra RK, Gupta SP. Increased bacterial adherence to respiratory epithelial cells in protein-energy malnutirion. Immunol Infect Dis 1990; 1:000-00 (in press).

45. Chandra RK, Dayton DH. Trace element regulation of immunity and infection. Nutr Res 1982; 2:721-733.

46. Beisel WR. Single nutrients and immunity. Am J Clin Nutr 1982; 35:417-68.

47. Chandra RK, Puri S. Trace element modulation of immune responses and susceptibility to infection. In: Chandra RK, ed. Trace elements in the nutrition of children. New York: Raven Press, 1985; 87-105.

48. Bendich A, Chandra RK, eds. Micronutrients and immune functions. New York: New York Academy of Sciences, 1990.

49. Gross RL, Newberne PM. Role of nutrition in immunologic responses. Physiol Rev 1980; 60:188-302.

50. Chandra RK. Trace elements and immune responses. In: Chandra RK, ed. Trace elements in the nutrition of children II. New York; Raven Press, 1991 (in press)

51. Chandra RK. Micronutrients and immune functions, an overview. Annals NY Acad Sci 1990; 587:9-16.

52. Nauss KM, Phus C-C, Ambrogi L, Newberne PM. Immunological changes during progressive stages of vitamin A deficiency in the rat. J Nutr 1985; 115:109-18.

53. Chandra RK, Au B. Single nutrient deficiency and cell-mediated immune responses. III. Vitamin A. Nutr Res 1981; 1:181-5.

54. Chandra RK. Increased bacterial binding to respiratory epithelial cells in vitamin A deficiency. Brit Med J 1988; 297:834-35.

55. Friedman A, Sklan D. Antigen-specific immune respnse impairment in the chick as influenced by dietary vitamin A. J Nutr 1989; 119:790-95.

56. Sommer A. Vitamin A status, resistance to infection, and childhood mortality. Ann NY Acad Sc 1990; 587:17-23.

57. Robson LC, Schwartz MR. The effects of vitamin B6 deficiency on the lymphoid system and immune responses. In: Tryfiates GP, ed.

Vitamin B6 metabolism and role in growth . Westport : Food Nutr Press, 1980; 205-222.

58. Chandra RK, Puri S. Vitamin B6 modulation of immune responses and infection. In: Reynolds RD, Leklem JE, eds. Vitamin B6 . Its role in health and disease. New York: Alan Liss, 1985; 163-75.
59. Sudhakaran L, Chandra RK. Vitamin B6 and Immune regulation. Ann NY Acad Sc 1990; (in press)
60. Anderson R, Smit MJ, Joone GK, van Staden AM. Vitamin C and cellular immune functions. In: Bendich A, Chandra RK. Micronutrients and immune functions. New York: New York Academy of Sciences, 1990; 34-48.
61. Pekarek RS, Sandstead HH, Jacob RA, Barcome DF. Abnormal cellular immune responses during acquired zinc deficiency. Am J Clin Nutr 1979; 32:1666-71.
62. Chandra RK, Au B. Single nutrient deficiency and cell-mediated immune responses. I. Zinc. Am J Clin Nutr 1980; 33:736-38.
63. Fraker PJ, Zwicki CM, Luecke RW. Delayed type hypersensitivity in zinc deficient adult mice. Impairment and restoration of responsivity to dinitroflurobenzene. J Nutr 1982; 112: 309-13.
64. Chandra RK, Heresi G, Au B. Serum thymic factor activity in deficiencies of calories, zinc, vitamin A and pyridoxine. Clin exp Immunol 1980; 42:332-35.
65. Prasad AS, Meftah S, Abdallah J, *et al.* Serum thymulin in human zinc deficiency. J Clin Invest 1988; 82:1202-10.
66. Chandra RK. Acrodermaatitis enteropathica. Zinc levels and cell-mediated immunity. Pediatrics 1980; 66:789-91.
68. Vyas D, Chandra RK. Thymic factor activity, lymphocyte stimulation response and antibody-forming cells in copper deficiency. Nutr Res 1983; 3:343-50.
69. Babu U, Failla ML. Superoxide dismutase activity and blastogenic response of lymphocytes from copper-deficient rats fed diets containing fructose or corn starch. Nutr res 1989; 9:273-282.
70. Vyas D, Chandra RK. Functional implications of iron deficiency. In: Stekel A, ed. Iron nutrition in infancy and childhood. New York: Raven Press, 1984; 45-59.
71. Hershko C, Peto TEA, Weatherall DJ. Iron and infection.Brit Med J 1988; 296:660-64.
72. Chowdhury BA, Chandra RK. Biological and health implications of toxic heavy metal and essential trace element interactions. Prog Food Nutr Sci 1987; 11:55-113.
73. Chowdhury BA, Friel JK, Chandra RK. Cadmium-induced immunopathology is prevented by zinc administration in mice. J Nutr 1987; 117:1788-1794.
74. Chowdhury BA, Chandra RK. Effect of zinc administration on cadmium-induced suppression of natural killer cell activity in mice. Immunology Letters 1990 (in press)
75. Jose DG, Good RA. Quantitative effects of nutritional essential aminoacid deficiency upon immune responses to tumors in mice. J exp Med 1973; 137:1-9.
76. Coovadia HM, Soothill JF. The effect of amino acid restricted diets on the clearance of ^{125}I-labelled polyvinyl pyrrolidone in mice. Clin exp Immunol 1976; 23:562-567.
77. Chuang JC, Yu CL, Wang SR. Modulation of human lymphocyte proliferation by amino acids. Clin exp Immunol 1990; 81:173-176.
78. Chandra RK, Baker M, Au B,

Whang S. Effect of two feeding formulas on response to challenge with Listeria monocytogenes in mice. Immunology Letters 1991 (in press)

79. Reynolds JV, Daly JM, Zhang S, *et al.* Immunomodulatory mechanisms of arginine. Surgery 1988; 104:142-51.
80. Erickson KL, Adams DA, McNeill CJ. Dietary lipid modulation of immune responsiveness. Lipids 1983; 18:468-474.
81. Murray Ge, Patrick J. Effect of dietary fat on sodium transport and sodium-lithium countertransport in rat erythrocytes and thymocytes. J Nutr 1986; 116:1390-1394.
82. Gogos CA, Kalfarentzos FE, Zoumbos NC. Effect of different types of total parenteral nutrition on T-lymphocyte subpopulations and NK cells. Am J Clin Nutr 1990; 51:119-122.
83. Barone J, Hebert JR, Reddy MM. Dietary fat and natural-killer-cell activity. Am J Clin Nutr 1989; 50:861-867.
84. Olson LM, Visek WJ. Kinetics of cell-mediated cytotoxicity in mice fed diets of various fat contents. J Nutr 1990; 120:619-624.
85. Erickson KL, Adams DAm Scibienski RJ. Dietary fatty acid modulation of murine B-cell responsiveness. J Nutr 1986; 116:1830-1836.
86. Meydani SN, Barklund MP, Liu S *et al.* Vitamin E supplementation enhances cell-mediated immunity in healthy elderly subjects. Am J Clin Nutr 1990; 52: 557-63.
87. Chandra RK. Fetal malnutrition and postnatal immunocompetence. Am J Dis Child 1975; 125:450-55.
88. Moscatelli P, Bricarelli FG, Piccinini A, Tomatis C, Dufour MA Defective immunocompetence in foetal malnutrition. Helvet Paediaat Acta 1976; 31:241-247.
89. Chandra RK, Ali S, Kutty KM, Chandra S. Thymus-dependent lymphocytes and delayed hypersensitivity in low birth weight infants. Biol Neonate 1977; 31:15-18.
90. Chandra RK, Matsumura T 1979 Ontogenetic development of immune system and effects of fetal growth retyardation. J Perinat Med 7:279-287.
91. Chandra RK. Serum thymic hormone activity and cell-mediated immunity in healthy neonates, preterm infants and small-for-gestational age infants. Pediatrics 1981; 67:407-11.
92. Chandra RK. Serum levels and synthesis of IgG subclasses in small-for-gastation low birth weight infants and in patients with selective IgA deficiency. Monograph Allergy 1986; 20:90-99.
93. Chandra RK. Interactions between early nutrition and the immune system. In: Barker DJP, Whelan J, eds. The childhood environment and adult disease. Ciba Foundation Symposium 156. London: Wiley, 1991 (in press)
94. Chandra RK. Antibody formation in first and generation offspring of nutritionally deprived rats. Science 1975; 190:289-290.
95. Beach RS, Gershwin ME, Hurley LS. Gestational zinc deprivation in mice. Persistance of immunodeficiency for three generations. Science 1982; 218:469-72.
96. Robson LC, Schwarz MR. Vitamin B6 deficiency and the lymphoid system. Effects of vitamin B6 deficiency in utero on the immunological competence of the offsping. Cell Immunol 1975; 16:145-156.
97. Chandra RK. Long-term health consequences of early infant feed-

ing. In: Atkinson SA, Hanson LA, Chandra RK, eds. Breastfeeding, nutrition, infection and infant growth in developed and emerging countries. ARTS Biomedical Publishers, St. John's, Newfoundland, 1990; 46-55.

98. Chandra RK. Nutritional regulation of immunity and risk of infection in old age. Immunology 1989; 67:141-47.

99. Chandra RK, Au B. Spleen hemolytic plaque forming cell response and generation of cytotoxic cells in genetically obese (C57Bl/6J ob/ob) mice. Int Arch Allergy Appl Immunol 1980; 62:94-98.

100. Pasulka PS, Bistrian BR, Benotti PN, Blackburn GL. The risks of surgery in obese patients. Ann Intern Med 1986; 104:540-46.

101. Chandra RK, Kutty KM. Immunocompetence in obesity. Acta Paediatr Scand 1980; 69:25-30.

102. Gurr MI. The role of lipids in the regulation of the immune system. Prog Lipid Res 1983; 22:257-87.

103. Johnston PV, Marshall LA. Dietary fat, prostaglandins and the immune response. Prog Food Nutr Sci 1984; 8:3-35.

104. Yumura W, Hattori S, Morrow WJW, *et al.* Dietary fat and immune function. J Immunol 1985; 135:3864-68.

105. Chandra RK. Dietary factors in immune responsiveness. In: Beare-Rogers J, ed. Dietary fat requirements in health and disease. Champaign, Illinois, American Oil Chemists Society 1988; 143-49.

106. Kelley VE, Feretti A, Izui S, Strom TB. A fish oil diet rich in eicosopentaenoic acid reduced cycloxygenase metabolites and suppresses lupus in MRL-lpr mice. J Immunol 1985; 134:1914-19.

107. Kulkarni AD, Fanslow WC, Rudolph FB, van Buren CT. Modulation of delayed hypersensitivity in mice by dietary nucleotide restriction. Transplantation 1987; 44:847-49.

108. Chandra RK. Excessive intake of zinc impairs immune responses. JAMA 1984; 252:1443-46.

109. Puri S, Chandra RK. Nutritional regulation of host resistance and predictive value of immunologic tests in assessment of outcome. Pediat Clin A Amer 1985; 32:499-516.

110. Chandra RK. Nutrition and the acquired immune deficiency syndrome. WHO Document, 1989.

111. Jain VK, Chandra RK. Does nutritional deficiency predispose to acquired immunodeficiency syndrome? Nutr Res 1984; 4:537-42.

112. Winick M, Andrassy RJ, Armstrong D, *et al.* Guidelines for nutrition support in AIDS. Nutrition 1989; 5:39-46.

113. Chandra RK, Puri S. Nutritional support improves antibody response to influenza virus vaccince in the elderly. Brit Med J 1985; 291:705-6.

114. Wallsh JA. Establishing health priorities in the developing world. New York, United Nations Development Program, 1988.

115. Ogra PL, Greene HL. Human milk and breast feeding. An update on the state of the art. Pediatr Res 1982; 16:266-71.

116. Victora CG, Vaughan JP, Lambardi C, *et al.* Evidence for protection by breast feeding against infant deaths from infectious diseases in Brazil. Lancet 1987; ii:319-21.

117. Chandra RK. Prospective studies on the effect of breast feeding onincidence of infection and allergy. Acta Paediatr Scand 1979; 68:691-94.

118. Briend A, Wojpynika B, Rowlands MJ. Breast feeding, nutritional state and child survival in rural Bangladesh. Brit Med J 1988; 296:879-882.

119. Grant WP. The state of the world's children 1990. Oxford: Oxford University Press, 1990.

Proc 6th ACN 1991: 62-76

Human energy requirements

W Philip T James and Ann Ralph

Rowett Research Institute, Aberdeen, UK

Introduction

There has been a remarkable surge in interest in the energy needs of children and adults since an expert group of nutritional scientists met in Rome in 1981 on behalf of FAO, the WHO and UNU to re-evaluate data on both protein and energy requirements. As Chairman of the energy sub-group I was privileged to be part of the development of a coherent approach to energy needs, which hitherto had been considered logically by very few nutritionists worldwide. Historically we have to remember that the use of the Douglas bag and other systems for measuring an individual's basal metabolic rate (MBR) had produced an amazing amount of data during the first few decades of this century. However, the question of how to encompass the problem of individuals' variable physical activity only emerged after the war. Dr Reg Passmore, whose training started in nutrition in India where he was for a short time in charge of the Coonoor laboratories, was the first to recognise the potential usefulness of a machine which Hugh Magee, Nutrition Adviser in the Ministry of Health, had discovered after the war in Germany (1). This apparatus had been built by Kofranyi and Michaelis and used extensively in Germany to measure energy expenditure in industry but was unused elsewhere until Passmore, with Durnin and Garry in Scotland, applied it systematically to document the energy needs of miners and of housewives and army recruits (2,3,4). Durnin with colleagues then measured, using both Douglas bags and the K-M system, the energy expenditure of groups of people throughout the world. One example of this was the survey undertaken by Norgan and Ferro-Luzzi in New Guinea in 1970 as part of Durnin's contribution to the International Biological Programme (5). Those of us who entered the energy field after this phase slowly came to realize why Passmore held such rigid views on energy balance (6) as we ourselves discovered the remarkable consistency of enery expenditure. Passmore and Durnin wer by now the leading authorities on energy needs (7) so it is little wonder that in the earlier FAO meetings on protein and energy requirements they simply specified the calorie needs of adults on a weight basis, and defined these for light, medium and heavy activity adults without documenting the basis for their decisions. Interest was anyway concentrated on the controversy of how much protein was required, so energy issues were neglected.

The UN consultation on energy needs in 1981

By 1981 we were ready to look at the problem afresh. So for a week we attempted to sort out our concepts. What do we mean by need ? If we simply measure what people eat then they may, in practice, be inadequately fed for healthy living. Thus emerged our first concept that it is unwise to use food intake values as a measure of energy requirements since the subjects

studied could be malnourished, ill or biochemically and behaviourally adapted to low food intakes. The "need for what?" question then dominated our thinking as we explored what we use our energy for. Clearly energy is used for basal metabolism, for processing and storing food and for physical activity. These three components had been reasonably well documented and we already had data from our calorimeters in Cambridge showing the remarkable consistency of an individual's metabolic rate over a 24 h period provided the physical activity was standardised. We could also condense all the data on daily energy expenditure if we expressed both the response to diet and activity together as a ratio of the BMR. So the problem was how to obtain clear evidence on the BMR and activity patterns of children and adults worldwide and then find a method of collating data on the energy cost of physical activity.

Previous Committees tended to rely on US data on BMR but these need not be representative. So Durnin and Francois (from FAO) undertook a preliminary analysis of worldwide BMR data which Durnin had initially selected. Then we would need to build up a picture of activity patterns based on Passmore and Durnin's approach of monitoring how people spent their time and how much energy was involved in a myriad of activities. This seemed impossible because people change their activity from one day to another, people's jobs differ and leisure time activity, such as gardening, communal work and sports, is highly variable. Furthermore, Ferro-Luzzi was insistent that we had to recognise the social demands for physical activity. If people were underfed they might compensate by sacrificing many extra activities of indirect benefit to their families and community. Thus we moved towards a principle of recognising that in specifying requirements we must identify the optimum needs for a "desirable" level of physical activity.

If, however, we were to specify desirable activities we must also establish "desirable" body weights. In affluent societies it was disadvantageous to be overweight and obese and we all recognized that low body weights in semi-starved adults were also likely to be a problem. Thus we found ourselves unable to justify the earlier recommendations on energy needs based on the per kg body weight values of light, medium and heavy activity individuals. This use of body weight implied that any weight was satisfactory.

One issue of great concern to FAO was how to cope with what Sukhatme claimed was the ability of man to adapt to low intakes at no cost to his welfare. This costless adaptation stemmed from an analysis of Sukhatme and Margen (8) which sought to develop biological principles from a statistical analysis of the intra- and inter-individual variability in food intake and energy expenditure. In Rome I argued against that concept but it was still used in FAO's 5th World Food Survey (9) and has been considered elsewhere (10). Sukhatme still finds the idea fascinating (11) but several of us have questioned both the statistical and biological plausibility of the idea (12,13,14). In 1981 we proposed that costless adaptation be ignored as of limited relevance when assessing energy requirements.

Although an approach based on energy expenditure seemed eminently suitable for adults we soon recognised that there were few coherent data on children's energy needs based on their BMRs, activity patterns and the physical cost of each of their many activities. We therefore had to rely on intake data obtained on healthy, active, well-growing children. The children's and adult data then had to be collated to obtain either household or national values for

energy needs.

Working through all these principles in the 1981 meeting took a week and with a further week in hand we then had to develop these ideas, collate whatever data were available and produce a coherent account for the UN Agencies. The data collation was then dependent on Ferro-Luzzi and Durnin but it soon became apparent that there were few published papers on how well or poorly nourished people used their time. Almost all the papers published simply summarised the energy cost of a day's activity so this could not readily be disaggregated. Expressing all the data in terms of the BMR was also new and often there were no separate BMR data in the published studies. As our time expired we also realised that our strategy of specifying energy needs on the basis of desirable activities for people of a desirable weight for height had led to estimated Asian food needs being increased by about 30% ! Clearly with such large issues of world agricultural policies and development linked to perceived food needs, we had to get our facts right. The 1981 FAO/WHO/UNU meeting therefore broke up with a clear idea of the principles we should use but with great concerns about the general applicability of the data on body weights, BMRs, activity patterns and the energy costs of physical activity. Eventually, after a further three years' work, new collations of data on BMR emerged (15) and the report from the UN meeting was eventually published in 1985 (16).

Following this we attempted to simplify the system of estimating energy requirements. Travis developed simple computer programmes to speed the calculations and we made the scheme more practicable by providing simple ways for estimating food needs by basing estimates on statistical data of occupational profiles and population age distributions. A range of allowances could also be applied. These allowances, e.g. for desirable physical activity, then matched the allowances used by nutritionists when dealing with the needs for other nutrients. The distinction between **prescribing** an energy need on the basis of what people should do and the actual energy being used was then clear. The manual for planners and nutritionists is now published (17) and available in several languages.

A simplied scheme for energy requirements

Table 1 lists the equations for calculating the BMRs of children and adults, the data on the elderly having been updated by ourselves with substantial new information on Europeans collected by Ferro-Luzzi and her colleagues in Italy; additional data on men were also provided by Durnin. In the 1980s we took a BMI (weight in kg divided by the square of the height in metres) range of 20.1-25 as the desirable weight range for men and 18.7-23.8 for women. These values were calculated from American Insurance statistics data when compiling the Obesity Report for the British Royal College of Physicians (19). The validity and usefulness of these reference values for Asia will be considered later. Table 2 then specifies the energy allowance which can be used for different age and population groups, these allowances being expressed as physical activity levels and therefore as a ratio to the estimated BMR of the group. Intake data had to be used, as already noted, for children under the age of 10 years. The effect of including allowances for infection in less developed countries (LDC) and for desirable physical activity in both LDC and developed communities can be seen by comparing the allowance and requirement figures. In general the difference amounts to about 5%. Table 2 shows that the allowance for infections only

TABLE 1
Equations for calculating the basal metabolic rate (BMR) of children and adults from their body weights (W) in kg

	Age range in years	MJ/day	kcal/day
Males	10-17	BMR = 0.0732W + 2.72	BMR= 17.5W + 651
	18-29	BMR = 0.0640W + 2.84	BMR= 15.3W + 679
	30-59	BMR = 0.0485W + 3.67	BMR= 11.6W + 879
	>60	BMR = 0.0565W + 2.04	BMR= 13.5W + 487
*	60-74	BMR = 0.0499W + 2.93	BMR= 11.9W + 700
	75+	BMR = 0.0350W + 3.43	BMR= 8.4W + 820
Females	10-17	BMR = 0.0510W + 3.12	BMR= 12.2W + 746
	18-29	BMR = 0.0615W + 2.08	BMR= 14.7W + 496
	30-59	BMR = 0.0364W + 3.47	BMR= 8.7W + 829
	>60	BMR = 0.0439W + 2.49	BMR= 10.5W + 596
*	60-74	BMR = 0.0386W + 2.88	BMR= 9.2W + 688
	75+	BMR = 0.041W + 2.61	BMR= 9.8W + 624

* New equations derived from European data (18). The other equations are the original listed by FAO/WHO/UNU (16).

applies to children up to the age of 2 years; thereafter the immunie state of the child can be expected to reduce the impact of microbial and other environmental hazards. These values are not adjusted to take into account the need for prolonged catch-up growth in stunted children. This is an additional judgement that nutritionists or agencies should make when deriving their population needs.

The different types of allowances are illustrated in Figure 1 which is based on the estimated needs of a 1-year-old group of Asian children. In addition to the energy cost of infection there is a need for additional energy to allow for a greater growth in height in Asian children should environmental conditions and perhaps protein intake improve. There is a small component also for the recognised low weight for height of some Asian children and the allowance for desirable activity amounts to about 5% of the total energy need. It is important to note that these prescriptive allowances add about 30% to the total estimated energy needs of the children. In practice therefore the average 1-year-old Indian child may be expected to be eating the equivalent of 921 kcal per day whereas to cope with the environmental stresses, to grow well and to sustain the activity necessary to explore their environment, learn and develop optimally it is suggested that these children need 1196 kcal per day. Figure 2 illustrates the impact of these allowances on natural energy needs in an Asian country such as India with its population structure. The likely impact in the long term of better growth in Indian children is also evident because as the stature of the young increases there will be a progressive rise in the average height of adults and therefore, given an appropriate weight for that greater height, an increase in energy requirement is to be expected. The outcome of all these calculations will be considered in the final section.

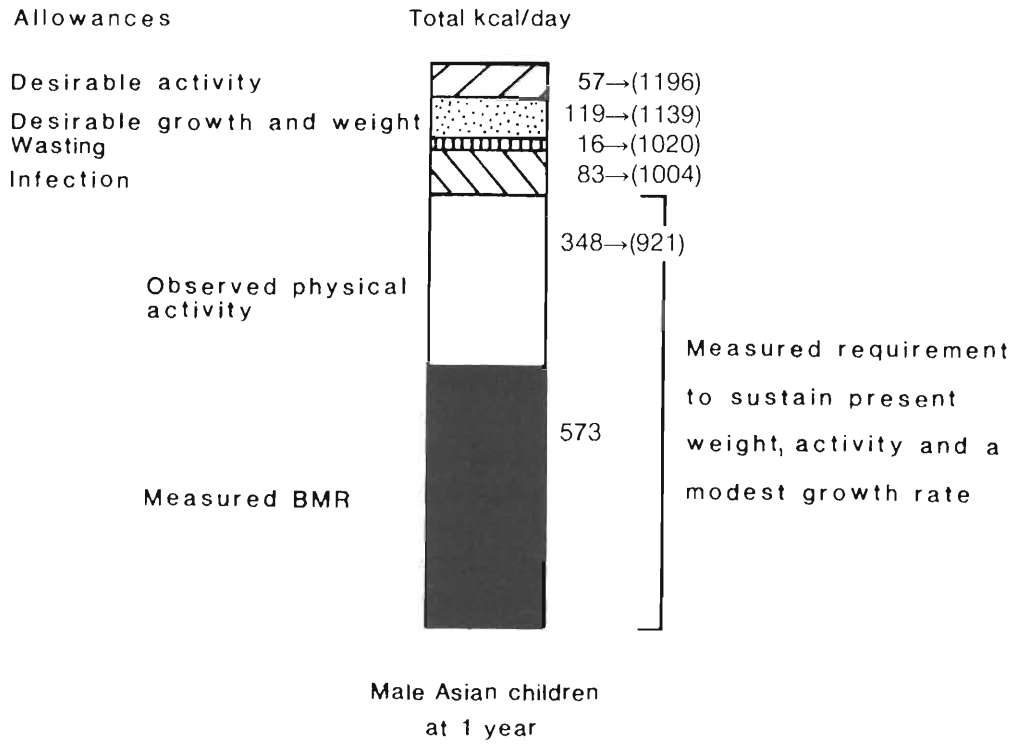


FIG. 1 An example of individual allowances for children.

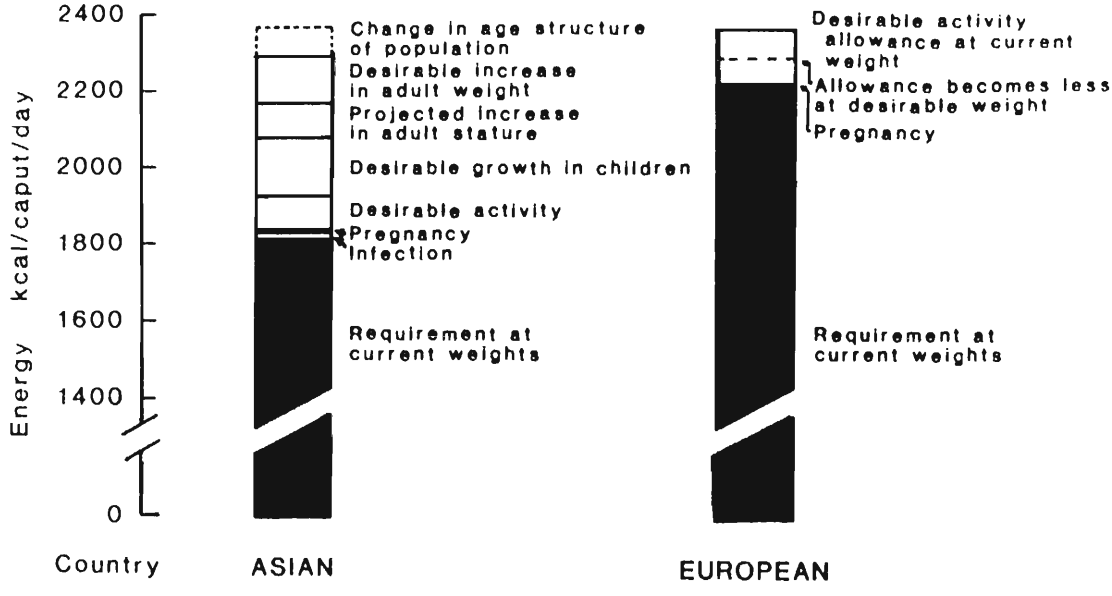


FIG. 2 Impact of different allowances on currennt national energy needs. The data include a pregnancy allowance calculated according to the original 1981 analysis which now needs to be modified in the light of substantial new studies on the energy requirements of pregnancy (20). The latest value proposed by the UK Government is 200 kcal/day and applies to healthy women of normal body weight only for the last trimester of pregnancy. This probably does not apply to Asian needs.

TABLE 2
Estimated desirable energy allowances and requirements. Children's data are given in terms of intake per kg body weight. Adult needs are expressed as physical activity levels (PALs) which are ratios of BMR

	Males		Females	
	Allowances	kg/cal Requirements	Allowances	kg/cal Requirements
0+	109/103*	98	109/103*	98
1+	108/104	99	113/108	103
2+	104	99	102	97
3+	99	94	95	90
4+	95	90	92	87
5+	92	87	88	84
6+	88	84	83	79
7+	83	79	76	72
8+	77	73	69	66
9+	72	68	62	59
		PALs		
10+	1.76	1.74	1.65	1.59
11+	1.72	1.67	1.62	1.55
12+	1.69	1.61	1.60	1.51
13+	1.67	1.57	1.58	1.47
14+	1.65	1.49	1.57	1.46
15+	1.62	1.44	1.54	1.47
16+	1.60	1.40	1.52	1.48
17+	1.60	1.40	1.52	1.50
Adults (18-59 yrs)	1.82/1.66 Light	1.41	1.67/1.60 Light	1.42
	Medium	1.70	Medium	1.56
	Heavy	2.01	Heavy	1.73
> 60	1.51	1.4	1.56	1.40

* The second figures refer to allowances for children or adults in developed countries where the needs for coping with infections and catch-up growth are excluded. The requirement figures are those where desirable physical activity has been removed from the estimated allowances of groups living in the developed world. The adults are classified into newly specified groups with light, medium and heavy activity patterns. The adult integrated allowances figures are crude estimates of likely activity of an appropriate mix of urban and rural communities in developing countries. Full details and explanation are given in James and Schofield (17).

Sex differences in allowances and requirements

Table 2 also shows that the energy needs of boys and girls differ from an early age; this reflects differences in body composition from infancy onwards, boys having a larger muscle mass and generally being more physically active. This early distinction persists throughout adolescence and

into adult life with the somewhat surprising observation that adult men and women have different PAL values implying that men are physically more energetic and sustain higher energy outputs when they are working than women. Yet the emphasis in the UN system now is on the problems of women who are perceived to be under intense pressure in many parts of the world as they carry the responsibilities for maintaining the home, for preparing and cooking food and for childbearing as well as contributing a major part of the agricultural activity in many countries. A recent study by Shetty, Ferro-Luzzi and their colleagues, conducted as part of a programme for the International Food Policy Institute, showed clearly that women did spend more time than men working in both India and Ethiopia. Furthermore the more deprived sector of the communities had men and women who were chronically energy deficient. The women sustained their domestic work and other work more diligently than the men who, when very thin, i.e. with a BMI < 16.0, were very inactive.

These data do not imply that the 1985 Report on energy requirements is wrong in relation to men's work because they may work more intensively than women. Clearly there is a need for more coherent analyses of time use and adults' energy demands for living.

Table 3 shows a simple scheme for calculating the energy needs of groups of adolescents or adults. The time allocated during the day to each type of

TABLE 3
The scheme for calculating the energy allowances of adults in absolute terms or as a physical activity level

	Time taken hours	Ratio energy cost to BMR	Energy need for each task KJ or kcal
1. Sleep	e.g. 7	1.0	
2. Work activity	e.g. 6	1.6-5.1	
3. Household tasks	e.g. 1-2	1.6-1.8	
4. Socially desirable activities	e.g. 1-2	2.5-3.3	
5. Cardiovascular maintenance	e.g. 0.3	4.0 or 6.0	
6. Residual time needs	e.g. 7-8	1.2-1.4	
			Sum

Divide Sum by 24 h BMR value to given average energy allowances as a PAL.

Note: The description of activities is derived from the FAO/WHO/UNU Report as set out by James and Schofield (17). The energy cost values vary depending on the nature of the task but represent the estimated cost as a ratio to BMR of both pauses and actual work during each period. These integrated energy indices differ from the minute-by-minute cost listed (17). Cardiovascular maintenance is to preserve muscle mass and physical fitness, the value of 4.0 being applied only to those >60 years of age. The residual time is normally specified as 1.4 but recent unpublished data suggest that a value of 1.2 may be more appropriate. The BMR from Table 1 is normally divided by 24 to give hourly values for generating this Table; the final allowance figure expressed as a physical activity level (PAL) is simply the sum of energy costs divided by the 24h value for BMR. This approach to PAL calculations was used in generating Table 2.

activity can be estimated. Then the average energy cost for those periods of general activity has to be measured directly or estimated from tables given by James and Schofield (17). These activity components include prescriptive activities which the 1981 Committee thought appropriate for health. In practice, these prescriptive levels of activity for the designated reasons are rarely achieved in LDC or developed societies so we have to see these increments as allowances rather than innate requirements.

Low metabolic rates in Asians

In the original analyses for developing equations for estimating the BMR of adults it was noted that the Indian data were nearly 10% lower than the North Americian data. Despite this a single set of equations were developed for universal application. Since then Shetty and his colleagues (21, 22, 23) have amplified the pre-existing data set and shown very clearly that Indians do have a lower BMR even when steps are taken to study well-nourished individuals with a normal BMR. Shetty has concluded that perhaps half of the decrement may prove to be related to body compositional differences and half to climate. Henry has also collated other evidence to show that BMRs in several tropical counties are appreciably below those calculated by Schofield (24).

It has to be recognised that many of the Indian subjects measured as adults may well have been somewhat stunted and slow growing as children. It would not be suprising therefore if long-term effects on muscle mass or on the size of other organs were to become evident. On this basis one can adopt two strategies. First, one can recognise that if adequately nourished Asian adults have a BMI above 18.5 then they may still have a BMR below the reference mean. Thus for calculating current requirements the values obtained from Table 1 would need to be reduced by about 10% to accord with the observed BMR differences. Secondly, it seems best in long-term planning to presume that as the nutritional state of the population improves it is likely that the BMR of Indians and others will move closer to those observed in Europe and North America. These lower BMRs may be an example of a long-term nutritionally dependent programming of metabolism but this is very different from the concept of thermogenic flexibility and costless adapatation proposed by Sukhatme.

Desirable body weights, biological adapatation and chronic energy deficiency

When the 5th World Food Survey (9) came to apply these new approaches they were careful to include the Sukhatme theory as a possible phenomenon which, if true, would reduce the number of people in the world who were classified as malnourished. Two different figures were therefore given. It was recognised that if food was inadequate it was likely that adults would lose weight. This was deemed to be a simple, biological adaptation if weight was merely being reduced within the normal or desirable range. This, however, raised the important question of what the lower limits of normal weight should be.

When the International Dietary Energy Consultative Group (IDECG) met in Guatemala in 1987 the question was how best to define inadequate levels of energy intake, i.e. chronic energy deficiency (CED). Although some felt that this was impossible, three of us came up with a closely argued case for specifying three degrees of CED based on a combination of low BMIs and physical activity (Table 4). The physical activity component was included because to define CED on the basis of low body weights alone might mean that we would classify lean,

TABLE 4

The original basis for classifying adults as chronic energy deficient (CED)

Body Mass Index	<16.0	16.0-16.9		17.0-18.4		18.4-24.9
Physical activity level as ratio of BMR	-	<1.4	>1.4	<1.4	>1.4	-
Group	CED III	II	I	I	Normal	Normal

Note that it is the combination of a low BMI and low activity which is required to make the specification of CED grade progressive as body weight falls. In the revised classification no assessment of energy turnover is used and three categories of BMI alone below 18.5 are used to specify the grades of CED.

Taken from James *et al.* (25), later revised by Ferro-Luzzi *et al.* (26).

healthy and very active adults as having chronic energy deficiency. So a maintenance energy PAL of 1.4 was chosen: anybody in developing countries who ate less than 1.4 times their basal energy needs was in all probability adapted behaviourally to a low energy intake and thereby attempting to relate a low body weight to some functional impairment so that we could develop a justification for our choice of cut-off points based on morbidity rather than on mortality statistics data, valuable though the latter would be. The choice of BMI ranges was judged on the basis of body compositional data on the body's energy reserves as fat at each level of BMI and some preliminary data were also available on the probability of illness in a small group of Bangladesh men (25).

Subsequently Francois in FAO calculated the morbidity and activity patterns of men and women and clearly showed increasing behavioural adaptation and illness in those whose BMIs were below 18.5. We then embarked, for FAO, on a detailed analysis of BMI data from all over the world and encouraged the recalculation of data and re-evaluation of morbidity data which might allow us a clear evaluation of the usefulness of the chosen cut-off points in BMI.

Perhaps the most striking information yet obtained comes from the National Institute of Nutrition in Hyderabad, India. Naidu, Neela and Rao have recalculated data on women in Hyderabad who completed pregnancy at different body weights. Table 5, reproduced from a recent NIN Newsletter (27) shows startling evidence of the remarkable association of BMI with a low birth weight. Of even greater significance is the progressive increase in the proportion of low birth weight children in groups of mothers whose BMI falls below the "overweight" group shown in Table 5. These results are of exceptional importance because a small baby is more likely to be disadvantaged in its future life. On a social basis this is therefore of national significance and suggests that if anything our BMI criteria were too generous for women. Originally the only basis for retaining the same BMI cut-off points for women as men was based on our concern that the higher energy stores at equivalent body weight in women might be advantageous to them in pregnancy and particularly in lactation. Now we have clear evidence that a BMI of 18.5 is not too

TABLE 5
Material weight and birth weight in Hyderbad, India

BMI grade	<16	16-16.9	17-18.4	18.5-19.9	20-24.9	25-29.9	>30
#	4	6.6	22.8	27.4	35.5	3.4	0.2
Mean maternal height (cm)	151.9	151.4	151.2	151.2	151.0	151.5	151.7
Mean maternal weight (kg)	35.4	38.1	40.9	44.1	49.6	60.6	75.5
Mean birth weight (g)	2510	2573	2673	2771	2812	2972	2956
# below 2.5 kg	53.1	41.4	35.9	27.7	26.4	14.7	20.0
Risk ratio of low birth weight child*	2.02	1.58	1.37	1.05	1.0	0.56	0.95

* This is the ratio of babies with low birth weight in each category compared with those with mothers having a BMI of 20-24.5. The mothers' average haemoglobin did not differ significantly between the groups being 10.9 g/dl on average. The weights were obtained 24 h after delivery, thus explaining the lower prevalence of chronic energy deficiency than in the national samples of non-pregnant women. Extracted from (27).

high a value for women and that modestly low levels of BMI are associated with functional decrements.

Further striking data emerged from NIN this year with their brief publication of mortality data on Indian men whose BMIs had been measured 10 years before an assessment of survival was made. Again a progressive increase in mortality was shown with men below 16.0 BMI having a three-fold greater mortality rate than those with BMIs above 18.5 (28).

A simplification in the classification of chronic energy deficiency

While these re-evaluation were proceeding, re-analysis of Indian and African data was proceeding in both the Italian National Institute of Nutrition and at the Rowett Research Institute. Data from both the rural Indian and Ethiopian studies showed that many adult men and women were surprisingly inactive and that it was impossible to discriminate the adults who were consistently inactive since activity patterns were so variable. Furthermore, we came to recognise that food intake data cannot be used as a measure of potential physical activity because the large differences between individuals in their BMRs meant that at equivalent food intakes some members of the group with a high BMR would be able to do far less than those who had a low BMR. Thus we would have to reply on physical activity monitoring to establish the three CED grades if we persisted with this measure in classification scheme. We concluded that our concern not to specify very active, thin individuals as having CED was an unnecessary extra criterion. In practice, the choice of 1.4 times the BMR as the activity cut-off point meant that in Ethiopian studies it seemed totally arbitrary who would fall above or below the line and the effect of including the measure seemed

unhelpful. We also noted that our original classification in practice led to a very odd distribution of CED cases since we would expect a smooth progression with a few severe cases but increasing numbers of moderate and mild CED in a population. This expectation of a biologically even measure only applied if we relied on BMI data alone. We have therefore concluded that a simple classification scheme based on BMI data only should apply.

Preliminary data relating to India

Table 6 presents preliminary data from studies only a few of which reflect national samples. Nevertheless it seems clear that by concentrating solely on children's growth UN Agencies may have obtained a distorted picture of Indian food and health needs. The data are a cause for great concern. With about 800 million people different published samples suggest that 50-70% of the adult population is chronically energy deficient. This is of enormous significance for public policy. It cannot be argued that this widespread deficiency is spurious and simply reflecting the choice of cut-off points in an arbitrary classification scheme since the National Institute in Hyderabad has objective data in both men and women of functional deficits at levels corresponding to the chosen BMI ranges of CED. These parallel the other functionally related African studies analysed by

TABLE 6

Adult chronic energy deficient (CED) in India in the late 1980s

Grade of CED	III	II	I	Mean BMI
		%		
Men				
Pooled 10 state survey	9	13	28	18.6
Hyderabad villages	5	13	33	18.9
IFPRI rural village study	19	19	32	17.7
Urban affluent				24.6±3.4
Women				
Pooled 10 state survey 1988-1990	11	13	25	18.6
Hyderabad villages	10	15	33	18.4
IFPRI rural village study	16	18	27	18.0
EEC study : poor women	19	16	33	17.9
Urban affluent				23.8±2.9

Note: Only the Pooled study calculated by Naidu and colleagues at the National Institute of Nutrition for FAO can be considered representative. The Hyderabad village and EEC study data were kindly provided by Dr K Satyanarayana from the National Institute. IFPRI data were made available by Prof. A Ferro-Luzzi. The IFORI study was organised to look at a particularly disadvantaged community and only the poor women from the EC study are cited. The means + SD of the affluent urban adults are taken from Gopalan (30).

Francois for FAO. Furthermore, extensive studies on affluent Indians by the National Institute dispense with the idea that Indians are racially different in terms of stature and size: Indians well fed from birth and without recurrent infections seem to attain dimensions very similar to those of Caucasians. We have to conclude that we now need to rethink completely our approach to adult malnutrition. Policies relating to public health, health care, rural development and agricultural development must all be reconsidered to take account of this newly recognised feature.

Other Asian countries

Table 7 presents very preliminary data on other Asian communities. China seems to be very unusual in having a very narrow distribution of BMIs with only a small proportion of the population having Grade I or mild CED. For the rest of Asia we have only sproadic data except for Vietnam. The Japanese are soon likely to become predominantly overweight and obese as their dietary fat content rises but in Vietnam it is clear that about 28% of the adult population has CED. Data from Malaysia, Thailand and Pakistan are not representative but CED may not be such a problem. It is difficult to believe that Bangladesh is any better than India and it would be useful to have clear data on Afghanistan, Borneo, Burma, Cambodia, Indonesia, Laos, Nepal and Sri Lanka. The Philippines would also merit study and data from Taiwan have not yet been re-analysed.

Conclusions

We are now on the verge of a complete re-appraisal of our concepts of energy requirements. The precision of our analyses has improved substantially and we now seem to have a coherent strategy for assessing energy requirements. Basal metabolic rates for Asians may prove to be about 10% below international levels but this could well reflect long-standing nutritional deprivation. If our new concepts of energy needs are taken to include a

TABLE 7
The body mass index of some Asian populations

	Males		Females	
	Mean	% CED	Mean	% CED
China	21.1	11.3	21.6	13.3
India	18.6	50.0	18.6	49.0
Malaysia	22.0	11.0	21.7	15.0
Pakistan (Sind)	18.9	48.0	19.4	40.0
Vietnam	18.3	28.0	19.9	29.0

Data kindly provided in more extensive form to FAO by: China Dr Ge; India - National Institute, 10 state surveys; Malaysia - Noor and Hashim; Pakistan - Garcia and Alderman. Vietnamese data are published (29). Only the data from China, India and Vietnam (29) are based on national or regional sampling methods. age groups vary but data relating to 18-30 years old only have been included.

TABLE 8
A comparison of different estimates of the energy requirements for Indian adults

Estimate	1973 FAO	1991	1991	1991
Body weight	Actual	Actual	BMI=20	BMI=20
Activity	Moderate	Moderate	Moderate	PALs Table 2
Women	1724	1852	1904	1939
Men	2309	2576	2649	2708

Actual body weights and heights were taken from recent data provided by the National Institute of Nutrition in India to FAO and applied as specified to the estimates. The moderate activity of the 1973 Report specified 46 kcal/kg for men and 40 kcal/kg for women. The current estimates are based first on actual body weights for direct comparison but with the new BMR and PAL levels of the FAO 1985 report. Then the effect of a BMI of 20 for both sexes is calculated to minimise the probability of CED in either men or women, and finally the generalised PAL values from Table 2 are included; these values specified in James and Schofield (17) make different assumptions about the proportion of light, moderate and heavy activity workers in urban and rural communities.

higher level of physical activity to maintain desirable contributions to societal and personal welfare and if we also take into account our new ideas on body weight, then it is apparent from Table 8 that these are likely to make substantial demands on the national adult energy needs which will rise by about 15-17%. The issue of chronic energy deficiency in adults has been neglected because nutritionists have concentrated their efforts on the so-called vulnerable groups. Levels of CED in Asia are highly variable but in India are higher than in Africa. We need to re-appraise our concepts of nutritional need in the light of this new evidence.

Acknowledgements

Much of the work described would not have conducted without the support of FAO and the help of P. Francois and R. Weisell. IDECG also financed the meetings which led to the definition of chronic energy deficiency.

References

1. Passmore R. The Nutrition Society 1941-1991. CAB International on behalf of the Nutrition Society, 1991.
2. Garry RC, Passmore R, Warnock GM, Durnin JVGA. Studies on expenditure of energy and consumption of food by miners and clerks. Fife, Scotland, Spec rept ser. London: Medical Research Council, 1955.
3. Durnin JVGA, Blake EC, Brockway JM. The energy expenditure and food intake of middle-aged housewives and their adult daughters. Br J Nutr 1957; 11: 85-98.
4. Adam JM, Best TW, Edholm OG, Fletcher JG, Lewis HE, Wolff HS. The dietary intake and energy expenditure of recruits in the

British Army. Army Personnel res Comm 58/3, 1957 London: MRC.

5. Norgan NG, Ferro-Luzzi A, Durnin JVGA. The energy and nutrient intake and energy expenditure of 204 New Guinean adults. Phil Trans Roy Soc Lond B, 1974; 268: 309-48.
6. Pessmore R, Eastwood MA. Davidson & Passmore's Human Nutrition and Dietetics 8th ed. Edinburgh: Churchill Livingstone, 1986.
7. Durnin JVGA, Passmore R. Energy, work and leisure. London: Heinemann, 1967.
8. Sukhatme PV, Margen S. Models for protein deficiency. Am J Chin Nutr 1978; 31: 1237-56.
9. FAO 5th World Food Survey, 1985. Rome: FAO, 1987.
10. James WPT. Research relating to energy adaptation in man. In: Schurch B, Scrimshaw NS, eds. Chronic Energy Deficiency: consequences and related issues. Switzerland: International Dietary Energy Consultancy group (IDECG), 1988: 7-36.
11. Sukhatme PV. Nutritional adaptation and variability. Eur J Clin Nutr 1989; 43: 75-87.
12. Healy JR. Comments on adaptation. Eur J Clin Nutr 1989; 43: 209-10.
13. James WPT. A commentary on Sukhatme's theories. Eur J Clin Nutr 1989; 43:205-8.
14. Waterlow JC. Nutritional adaptation and variability. Eur J Clin Nutr 1989; 43: 203-10.
15. Schofield WN, Schofield C, James WPT. Basal metabolic rate - review and prediction, together with an annotated bibliography of source material. Hum Nutr Clin Nutr 1985; 39C, Suppl 1: 1-96.
16. FAO/WHO/UNU. Energy and protein requirements. Geneva: WHO, 1985. (Technical report ser. 724).
17. James WPT, Schofield EC. Human Energy Requirements. Oxford Medical Publications, 1990.
18. Department of Health. Dietary Reference values for food energy and nutrients for the United Kingdom. London: HMSO, 1991. (Report on Health and Social Subjects 41.)
19. Royal College of Physicians. Obesity report. J. Roy Coll Phys Lond 1983; 17: 1-58.
20. Durnin JVGA. Energy requirements of pregnancy: an integration of the longitudinal data from the five country study. Lancet 1987; ii: 1131-33.
21. Soares MJ, Shetty PS. Validity of Schofield's predictive equations for basal metabolic rates of Indians. Ind J Med Res 1988; 99: 253-60.
22. Shetty PS. Physiological mechanisms in the adaptative response of metabolic rate to energy restriction. Nutr Res Rev 1990; 3: 49-74.
23. Soares MJ, Shetty PS. Basal metabolic rate and metabolic economy in chronic undernutrition. Eur J Clin Nutr 1991; (in press).
24. Henry JK, Ress DG. In: Blaxter Kl, MacDonald I, eds. Comparative Nutrition: A preliminary analysis of basal metabolic rate and race. London: John Libbey, 1988; 149-62.
25. James WPT, Ferro-Luzzi A, Waterlow JC. Definition of chronic energy deficiency in adults. Eur J Clin Nutr 1988; 42: 969-81.
26. Ferro-Luzzi A, Sette S, Franklin M, James WPT. A simplified approach to assessing adult chronic energy deficiency. Eur J Clin Nutr 1991; (in press).
27. Naidu AN, Neela J, Rao NP. Maternal body mass index and birth

weight. Nutrition News 1991; 12: No. 2.

28. Satyanarayana K, Rao SS, Radhial G, Reddy V. BMI and mortality pattern - a 10 year retrospective study. Ind J Nutr Diet 1991; (in press).

29. Khoi HN. Protein-energy nutritional status of rural people in some regions of Vietnam. Warsaw: Instytut zywnosci, 1990.

30. Gopalan C. Overview and heights and weights of parents. In: Growth of affluent girls during adolescence. New Delhi: Nutr Foundation India. (NFI Sci Report 10.)

Proc 6th ACN 1991: 77-78

Modern techniques of amino acids production towards future nutritional needs

Ryuichiro Tsugawa
Ajinomoto Co., Inc. Tokyo, Japan

Owing to the recent progress in nutritional, physiological and medical fields, utilisation of amino acids as clinical nutrients and pharmaceuticals has been widely expanded. Studies on the wide application of amino acids have resulted in consumption of a large amount of amino acids as clinical nutrients and pharmaceuticals. This demand for amino acids has in turn accelerated the R&D of amino acids production and has led to the industrial production and the commercial supply of a variety of amino acids.

In this presentation, the technical progress of amino acids production and their possible techniques towards future nutritional needs are described.

A variety of purified amino acids is used for parenteral and enteral nutrition, and purified protein hydrolysate is also used for enteral nutrition in the field of clinical nutrition.

Recent R&D studies on the medicinal efficacy of amino acids in clinical nutrition has made clear the specified activities of amino acids against various kinds of diseases.

Branched chain amino acids, such as leucine, isoleucine and valine, are effective against hepatic encephalopathy and sepsis by infection. Such essential amino acids as arginine and histidine are effective against renal disorders, and glutamine is also effective in the patient who had an operation for enterectomy.

To meet the needs for stabilisation to heat and for higher solubility of amino acids, chemicals properties of their dipeptides are becoming important enough to solve these issues in the parenteral nutrition area. Heat-unstable amino acids, such as glutamine and cysteine, can be stabilised by converting them to corresponding dipeptides. In addition, poorly soluble amino acids, such as isoleucine, leucine, valine and glutamine can be modified to corresponding dipeptides in order to increase their solubility. The improvement of a method for the preparation of dipeptides at low cost is an important issue in amino acid-manufacturing industries.

Technical progress of amino acids production can be categorised into three periods. In the first period, amino acids were produced by extraction from hydrolysed protein. The present process which was developed in the second period is utilising wild strain or conventional mutants of bacteria in fermentation of enzymatic process. In this period, we also have created "the metabolic regulatory fermentation" in Japan. In the third period, microorganisms which were improved by recombinant DNA technique or cell fusion technique will be used in fermentation or enzymatic process.

In general, biosynthesis of L-amino acids in organisms are well balanced, and excessive production of L - amino acids is metabolically regulated by feedback inhibition by end-products inside the cells. In almost all cases of L-amino acids fermentation, therefore, microorganisms or key-enzymes

therein were necessarily desensitised to this feed-back inhibition except L-glutamic acid fermentation.

A method for desensitisation to feedback control by end-product is described, taking L-lysine-producing regulatory mutant as example.

In 1971 it was found that L-lysine analogue, aminoethyl cysteine resistant strain of this microorganism could produce large amounts of L-lysine in the culture medium, and after that, in the same way, amino acid analogue resistant strains could produce the respective amino acids.

In this way, many L - amino acid-producing mutants were obtained, and thus "the metabollic regulatory fermentation" was established.

Flow diagram of L-amino acid production by fermentation is described.

In order to supply large amounts of amino acids of high quality at economical price, trials for cost reduction in the manufacturing process are important. For the cost reduction, an improvement in fermentation yield of amino acids from sugar, carbon source, is one of the major factors. At present, the yields of L-glutamic acid, L-lysine, L-ornithine, L-glutamine and L-proline are fairly high compared with their theoretical yields. However, the yields of other essential L-amino acids such as L-histidine, L-isoleucine, L-leucine, L-phynylalanine, L-threonine, L-trytophan, L-tyrosine and L-valine are still lower. So the improvement in yield of these essential L-amino acids is necessary to provide large amounts of these amino acids at economical price. This is especially so for the production of the branched chain L-amino acids, because demand for these amino acids will be expected to increase in the future.

L-Aspartic acid, L-alanine and L-cysteine are produced by enzymatic methods from respective intermediate or precursor. L-cysteine is produced through a skillful method established by Ajinomoto Co., in which DL-amino thiazoline carboxylic acid is totally converted to L-cysteine.

As a method for improving the activity of L-amino acid-producing-bacteria, r-DNA technique is expected to get a higher level of yield than that of conventional mutant. Through the application of r-DNA techniques, the conventional mutants which gave lower L-amino acid yield, such as L-threonine, L-phenylalanine, L-tryptophan and L-isoleucine-producers, can be made to improve their productivities.

Owing to the recent progress in biotechnology, which includes r-DNA, mass cell culture and cell fusion techniques, we are able to get a considerable amount of physiologically-active proteins derived *in vitro* from human cells which are working physiologically in human body.

The purification process for these human proteins seems to be technically difficult to get them in their biologically-active or native form. However, if we can get large amounts of these purified proteins, we can use them for nutritional purposes. It will be important to have dipeptides of L-amino acids supplied as the high quality clinical nutrients. To date, however, the biotechnological techniques which can supply a large amount of these peptides at ecomonical price, have not been established.

"Tandem dipeptide cutting system", which is intended to cut off the same dipeptide one after another from the long chain of protein which is composed of the tandem dipeptide, and **"synthetic system by enzyme or living cell"** are proposed as possible methods for the dipeptide production.

Proc 6th ACN 1991: 79-91

Diet and naturally occuring human diseases caused by inadequate intake of essential trace elements

Guang-Qi Yang

Institute of Nutrition and Food Hygiene Chinese Academy of Preventive Medicine Beijing

Introduction

Among the 90 naturally occurring elements, 73 are termed as trace elements. At present, only 17 elements, Cr, Mn, Fe, Co, Cu, Zn, Se, Mo, I, F, Li, Si, V, Ni, As, Pb and B, are recognised as essential to man (1). Ten of these essential elements, i.e. Fe, Cu, Zn, Cr, I, F, Se, Mo, As, and B appear to have presented problems in normal human nutrition. The problems arose mainly either from dietary form (e.g. Fe, Cu, Zn, and Cr) or from geochemical environment (i.e. I, F, Se, Mo, As and B).Some of these diseases are of world-wide prevalence, imposing severe harm on human health. For instance, the nutritional iron-deficiency anaemia (IDA) is the most common nutritional disorder and is an important cause of morbidities, and when severe, mortality. In developing countries, severe anaemia can be an associated cause in 50% and the main cause in up to 20% of maternal deaths (2). Iodine deficiency desease (IDD) is another recognised problem of world-wide concern, and more than 3 million people are overt cretins and millions suffered from some intellectual or motor deficiency in parts of the world (3). Se-deficiency related diseases covered a very wide area in China. Among them, Se deficiency and Keshan disease (KD) have been well documented. Kashin-Beck disease (KBD) has also been reported to be Se-responsive.The severity of IDD may be enhanced by Se-deficiency. Problems of association of Se with cancer and cardiovascular diseases have not been resolved (4).

A close examination on the occurrence of these diseases would be useful for their prevention or for revealing unknown roles for the newer trace elements. For this purpose, disorders such as caused by man-made environmental pollution, genetic defects, other secondary effects and trace element (i.e. cobalt) whose nutritionally-available form is worked out as a vitamin by intestinal flora, are excluded in this discussion.

Essential trace elements differ from other micro-nutrients in that, they all come from the soil. But why the problem of cation group arises from nutritional reason and only anion group from geochemical environmental reason? Whether the imbalance state of such cations or not exists in soils. To understand the distribution of the cation group in soil, plant disease could be expected as an indicator. Although plants, in general, are much more resistant to an increased concentration than to an insufficient content of a given element (5), the exhibition of plant deficiency and poisoning diseases, or the verification of unusual levels of certain elements in plants, would at least show that the possibility of geochemical factors has an influence on the health of local people.

Naturally occurring plant diseases caused by insufficient or excessive supply of trace elements in cation group from local soil

Naturally occurring plant diseases related to deficiency of Fe, Cu and Zn were widespread, while Fe toxicity has constituted an economic problem in certain rice-growing areas (6). Some plant species are Cu- or Zn-tolerant (7); they accumulated these elements without manifestation of any toxic signs. However, toxicities of these to elements still appeared as plants grew in soils in the neighbourhood of ore deposits. Cr is not required by plants; thus environmental deficiency of Cr cannot be judged by plant deficiency disease. However, Underwood attributed the substantial variation of Cr levels in human liver and kidney as a reflection of regional difference in environments (8). Phytotoxicity of Cr, however, has been reported for plants on soils developed from ultra basic rocks. Native plants, mainly from areas of surpentine can accumulate as much as 0.3% Cr and forest trees grow poorly there (5). Therefore the natural influences of insufficiency and excess of Fe, Cu, Zn and Cr from soils on plants are in existence (Table 1).

Naturally occurring human diseases caused by inadequate intake of trace elements of the cation group from locally-produced foods

It is apparent that a distinct property of cation group is the low efficiency of absorption. As high as 70-99.8% of metals contained in foods cannot be absorbed (9-13). This property would largely reduce the bioavailable amounts in foods, thus greatly help to alleviate the risk of toxicity, but it would greatly enhance the risk of deficiency (Table 2). Fe and Zn deficiency diseases easily prevailed among people when cereal and vegetables were used as staple foods in particular, since Fe and Zn are

TABLE 1

Natural plant diseases of deficiency and toxicity caused by the soil imbalance state of cation group

	Deficiency	Toxicity
Fe	Chlorosis of leaves (WS) (Calcarous soild)	Brown spots in leaves (WS) (Rice growing area)
Cu	Exanthema Dis. (WS) Reclamation Dis. (WS)	Inhibition of root growth (Tol.)
Zn	Little-leaf Dis. (WS)	Inhibition of root growth Chlorosis of leaves (Tol.)
Cr	Not required	Chlorosis of leaves, brownish red leaves (basic rocks)

WS = Widespread
Tol. = Tolerance

poorly utilised in crude cereal products, while in highly polished cereals only poor amounts of these metals are retained. Iron-deficiency anaemia is a widespread disease, particularly among children from 7 months to 1 year of age. Even in the city of Beijing, the incidences, among 236 infants within the ages of 4 to 6 months were: nutritional anaemia 45.6%, iron deficiency 62.1% and iron-deficiency anaemia 34% (14). Zn deficiency is also a worldwide problem. A syndrome of Zn deficiency similar to nutritional dwarfism has been reported in Iran (11). Marginal Zn deficiency is likely a nutritional problem among children in China (15). As high as three hundred million or around one-third of the population of China is at risk of iodine deficiency disease (IDD) (16). Cu and Cr deficiencies appeared in malnourished children, while Cr may be deficient in some old people and diabetics.

Naturally occurring human diseases caused by inadequate intake of trace elements of the anion group from locally produced foods

An important reason of problems arising from anion group seems to be its high absorption efficiency (Table 3), in contrast to that of cation group. Both deficiency and toxicity diseases occurred for most members in anion group. As Mertz has pointed out that elements occurring in small anionic form are different from that of cationic form in some respects, homeostatic control is relatively weaker for anionic form, but the latter is more efficiently absorbed. However, their final bioavail-

TABLE 2

Naturally occuring human diseases caused by inadequate dietary intake of trace elements in cation group

Element	Efficiency of absorption	Deficiency disease	Prevalence	Toxicity
Fe	1-2% for cereal-dominated diet	IDA	Worldwide	?
Cu	Poor	Malnutrition	Recovering from PCM	?
Zn	20-30% for cereal-dominated diet	Nutritional dwarfism	Mild deficiency may be common	?
Cr(III)	0.2-0.5%	Impaired glucose tolerance	Malnourished children, diabetics etc.	?

IDA = Iron deficiency anaemia
PCM = Protein calorie malnutrition

abilities were further infuenced by dietary interactions (16,17). The differences in their behaviours may be attributed to the different physico-biochemical properties between cation and anion groups. In the anion group, in consequence of long-term intake of inadequate amounts of certain element(s), the organism will not be able to regulate and maintain tissue element concentration at normal range, and endemic diseases may appear. In areas where the main dietary components are locally-produced vegetables or where the drinking water is supplied by local wells, such a living style enables the geo-chemical imbalance state of soil to exert its influence on local inhabitants through foods (Table 3) and drinking water, and alter the normal metabolism. For instance, in Se-deficient area, corn and rice contained Se averaging less than 0.01 μg/g; if one takes 600 g of either cereal daily, the Se intake is only one-fourth of the minimum requirement, while if one takes 100 g of animal foods (fresh water and poultry products), it will

TABLE 3

Naturally occurring human diseases caused by insufficient or excessive dietary intake of trace elements in anion group.

Element	Absorption	Deficiency disease	Prevalence	Toxicity
I	Almost complete	Goiter, Cretinism	Worldwide	Goiter
F	Efficient	Dental caries, Osteoporisis	Public problem	Mottled teeth, skeleton, fluorosis, etc.
Se	Efficient	KD, (KBD) etc.	Widespread in China	Hair, nail loss
Mo	Ready	EC	In Linshan, China	Gout
As	Good	?	?	Abnormal pigmentation & keratosis of skin etc.
$B(OH)_3$	Almost	Osteoporosis Arthritis	?	?

KD = Keshan disease
KBD = Kashin-Beck disease
EC = Esophageal Cancer

supply more than three-fourths of the minimum requirement. On the other hand, one can find plant foods also contained the highest amounts of Se in high Se area. During outbreak of Se-toxicity, daily consumption of 600 g of corn or 400 g of turnip green alone can provide around 25 mg of Se which is more than forty times the proposed maximum safe Se intake of 550 µg/d in seleniferous area. Thus plant foods possesss great ability to bring about Se imbalance including either deficiency or toxicity or other relationships from interactions of ion in soils (Table 4).

soils. Iodine in drinking water generally reflects the iodine level of the local soil. In goitrous regions in Epypt, the water iodine content ranged only 7-18 µg/l (18). Long-term intake of insufficient iodine results in retardation of both physical and mental development. As high as 300 million or around 1/3 of the Chinese population is at risk of iodine deficiency disease (IDD) (19). Recently it is identified that the enzyme, type I iodo thyronine 5' - deiodinase which catalyses the deiodination of T4 to T3, is a selenoenzyme (20);

TABLE 4

Comparison of the capacities of vegetable and animal foods for transmittance of soil Se imbalance state (2,39,40,44-48)

	Se Concentration (µg per g or ml)		
	Low-Se area	Ordinary Se area	High-Se area
Environments			
Soil	0.112	0.234	7.9
Medium			
Corn	0.006	0.032	0.5-44.0
Rice	0.008	0.051	0.3-20.2
Vegetable (leafy)	0.0007	0.006	0.945-71.3
Kidney	0.613	2.17	0.74-3.72
Fish	0.168	0.469	4.1
Shrimp	0.171	0.274	-
Egg	0.120	0.213	2.77
Residents blood	0.019	0.093	3.2

Calculated on fresh basis

The iodine concentration in foods varied greatly and is influenced by the content and availability of iodine in

thus the concomitant deficiency in iodine and Se would aggravate iodine deficiency. Although it was found that

blood level of T3 in residents in low-Se area in China, is usually lower in comparison with that of T4 (21), whether or how it had affected IDD is not known. Iodine toxicity has been reported in Japan and China. In China toxicity can be caused either by consuming high iodine foods as in Japan or by drinking high iodine content water in high iodine area. High iodine areas are located both at coast and inland, sometimes in the neighbourhood of oil field. The iodine content of drinking water may be as high as 1920 μg/L where the incidence of goitre is 41% (22). Food iodine contributed much less amount to the daily iodine intake (Yu Z, 1991; personal communication).

Soil fluorine is not readily taken up by grain and thus fluorine in drinking water becomes an important source of human daily fluorine intake. Since the flourine content of drinking water varies from 0.1 to 40 μg/ml, flourine deficiency and toxicity are widespread diseases in many parts of the world. In China, endemic flourosis is particularly severe; it is caused either by drinking water of high flourine content or inhaling air contaminated by high F coal smoke. Flourine contents of drinking water in Chinese endemic areas were within the range of 1-4 mg/L, and in areas where heavy prevalence appeared, were > 4 mg/L. The highest content reached 32 mg/L (23). Prevention of flourosis has proved to be a difficult problem in practice in China, although various methods including improving living conditions, protecting from inhaling F-contaminated air, changing water sources and removing water flourine by physical and chemical methods have already been proposed.

Molybdenum content of grains is greatly influenced by Mo level and circumstances in soils. Deficiency of Mo in humans has been described in patient from prolonged TPN using amino acid solution with inadequate molybdenum whereby signs caused by deficency of two Mo-enzymes, sulphite and xanthine oxidases, appeared (24). Naturally occurring cases have not yet been found. However Mo was claimed to exhibit an inhibitory effect on carcinogenesis in an esophageal cancer high risk area where environmental Mo level is low (25), while high incidence of gout has been reported in high Mo area in Armenia, Soviet Union (26).

Soluble boron in the soil consists mainly of boric acid. Under soil pH conditions this acid does not dissociate and in contrast to all other plant nutrients, boron is mainly present in a nonionised form in soil solution. This may be the main reason why boron can be leached so easily from the soil. In contrast to humid areas, boron may accumulate in arid regions to toxic levels in the upper soil layer (7). Concentration of boron in drinking water varies considerably according to geographic source and may account for most of the total dietary intake (27). Boron was reported to affect calcium metabolism via a regulatory role and is an important nutritional factor determining the incidence of osteoporosis particularly under low dietary intake of magnesium or with hormonal changes, such as those in menopausal women that cause an increased loss of calcium from bone (28). Supplementation of a low-boron diet with boron induces changes in post-menopaused women consistent with the prevention of calcium loss and bone demineralisation (29). It is more concentrated in plant tissue than animal tissue (30). Since boron has a low order of toxicity and signs of chronic toxicity were not defined, whether or not boron toxicity has been a problem in certain areas on the world is not known.

The essentiality of arsenic to humans has not yet been well recognised. In the northern part of XingJiang where arsenic concentra-

tions in drinking water ranged from 0.05 to 0.85 μg/ml, the incidence rate of endemic arsenosis was reported to be over 45%. The symptoms are numbness of extremities, drowsiness, weakness, hyperkeratosis and abnormal pigmentation of skin (30).

Selenium deficiency and KD (31, 32, 33, 34, 35)

Early clinical, pathological and epidemiological studies have evidenced that KD is a biogeochemical disease, the occurrence of which is always associated with White Muscle Disease of animals. This indicated that KD may be a selemium deficiency-related biochemical disease. To identify KD with Se deficiency, two categories of work have been performed. (a) Poor Se level is associated consistently with geographical distribution of KD epidemiologically (31, 32, 33, 34). (b) KD is a Se-deficiency related nutritional deficiency endemic disease. The Se-poor environments depleted the residing inhabitants via long-term intake of locally- produced vegetable foods and consequently KD prevails regionally (Table 3). The disease can be prevented by Se-supplementation (Table 4) (35).

Along with the recent change of rural dietary habit, incidence of KD naturally fell toward its historical minimum year after year which led people to suspect whether Se is responsible for this reduction. A large scale observation was thus conducted in west China (36) (Table 5). The results indicated not only that Se is necessary but also that the intakes of selenium naturally increased and were in most cases not enough to meet requirements. Furthermore, it also reflected that KD is a multi-nutrient deficiency with Se-deficiency as the primary, fundamental factor, since KD occurred only in extremely low Se area.

TABLE 5

Efficacy of sodium selenite for prevention of Keshan Disease among vulnerable population in Sichuan province, west China (39)

Group	Year	Total Subjects	Case	Incidence (per thousand)	Dead	Blood Se level* (μg/ml)
Control	1974	3,985	54	13.6	27	0.014
	1975	5,445	52	9.5	26	
Treated	1974	4,510	10	2.2	0	0.052
	1975	6,767	7	1.0	1	
	1976	12,579	4	0.3	2	
	1977	12,747	0	0	0	

*Estimated after 6 months on oral Se-tablet

Based upon the above facts, a hypothesis for the incidence of KD (31,32,33) is summarised as follows: "KD is a biogeochemical disease. Poor Se state of soil has been demonstrated over the wide endemic areas as the geochemical factor (32). Inhabitants were depleted after long-term intake of low Se foods produced on the local soil, and finally they became Se-deficient. The presence of stress factor(s) in combination with Se-deficiency is able to start the cardiopathogenesis and the prevailing of KD. The combination factor(s) may vary as place is varied. They may be nutrients or non-nutrients originally existing or as foreign contaminants probably in grains attacking particularly the myocardium in synergyism with Se deficiency (38-40) resulting in increase of Se requirement". Recent studies on mechanism of myocardiopathogenesis revealed that the antioxidative ability of patients is weakened in consequence of Se-deficiency. Biomembranes and its intimate respiratory enzyme systems, and macromolecular substances in cardiomyocytes are damaged, the structural and functional alterations of the important constituents in cardiomyocytes and the resultant impairment of heart energy metabolism and muscle contraction would be responsible for the necrosis of heart muscle. The results obtained are in harmony with what the hypothesis has suggested.

Prevention of Se-deficiency diseases

Selection of foods

Prevention of deficiencies of trace elements of anion group cannot be achieved by selection of foods and is somewhat different from that of cation group. The influence of geochemical factors on food Se contents is so prevalent and intensive that the author was unable to find any satisfactory plant foods as dietary Se supplements through estimation of 47 species including farm and mountainous vegetables and fruits in low Se area (41). The only food found to contain satisfactory amount of Se was mushrooms ranging from 0.29 to 0.49 μg/g, however their Se is poorly available. Only animal foods such as poultry products, fish and shrimp contained significant amounts of Se. In low Se area domestic animal products, except kidney, such as meat and liver contained little Se (41). Since animal foods are used as dishes, the amounts usually ingested are not enough to raise the daily dietary Se intake to a satisfactory level (Table 3).

The importance of cereals

Cereals are always the key foods in the usual diets to contribute to the bulk of dietary Se intakes. People of coountries producing low Se cereals such as Finland and New Zealand had comparatively low dietary Se intakes even though the percentages of total Se intakes from animal foods were the highest. In the case of Japan, Se level in cereals was average and with sufficient dietary intakes of animal foods, the total dietary Se intake was able to reach the expected level. In the cases of United States and Canada, not only the Se levels in cereals but also animal foods consumed were high as well, and consequently their dietary Se intake became the highest, (42) while in the Chinese endemic rural diet, both Se levels in the cereals and animal foods were very low and as a result, the daily dietary Se intake was the lowest (Table 6). This indicates furthermore that, cereal can be used as an ideal vehicle for Se-supplementation.

Efficacies of different methods used to raise dietary Se intake in low Se areas in China

Increase in dietary Se intake in endemic area cannot be achieved by selection of foods or change of dietary

TABLE 6

Influence of Se-enriched table salt administration on the recent natural reduction of incidence rate of KD

Group	Total Subjects (million)	1980-1983		1984		1985		1986	
		Case	Rate	Case	Rate	Case	Rate	Case	Rate
Control	0.6	88-146	14.7-25.1	70	11.6	37	6.1	2.8	4.2
Se-treated	1.05	244-283	23.7-28.1	78	7.2	7	0.64	5	0.46

Adopted from Y.Y. Chen and P. Qian. Ref. (36).
Average incidence rate ($u=7.36$, $P < 0.0001$)

patterns (Table 7). Supplementation of Se to endemic people by addition of Se to either fertilizer or table salt was used in China. Se-enriched table salt was easily accepted due to its simplicity. However, since the Se added is of inor-

TABLE 7

Influence of Se concentration of cereals on the dietary Se intakes in different countries

	China	Finland*	New Zealand	Japan*	U.S.A*	Canada
Cereals						
Se level (μg/g)	<0.02	0.02	0.035	0.07	0.30-0.33	0.410
% dietary intake	70	10	9	27	34	48
Animal foods						
% dietary intake	<5	86	84	66	62	46
Total dietary intake (μg/d)	7	30	32	88	132	201

Dietary intake proposed: (μg/d)	Minimum	Adequate	Maxim
	22	50	400-550

* Adopted from Combs and Combs (41)

ganic form which cannot be stored in the body, its ability to raise body Se status is limited. Therefore administration of Se to fertilizer to increase cereal intake and the preventive method mentioned above, the suggested cereal safe concentration (0.5 to 0.8 μg/g) could be obtained (Table 8).

TABLE 8

Efficacies of dietary patterns or food Se concentration limitations used to raise or reduce daily dietary intake in low and high Se areas

Area	Actual dietary (μg)	Diet ary pattern*			Se-Enrichment**	
		Western (μg)	Japanese (μg)	American (μg)	Cereal 0.04-0.10 (μg/g)	Table salt (μg/g)
Low Se	7	13	12	20	20- 44	50
High Se	4990	>3945	-	-	400-549**	-

* Adopted from Combs and Combs (41)

** Suggested Cereal Se level 0.5-0.8 μg/g (42).

Se content to 0.04-0.10 μg/g or a predicated daily Se intake of 20-50 μg/d is the method of choice (43). In this respect, Finland had successful experience. As a result of enrichment of fertilizers with Se, the mean serum Se level of Finnish people was found to increase from 70 to 110 μg/L between 1984 and 1987 (44).

Prevention of Se toxicity (44)

It is important first to prevent the contamination of foods and soils from high Se coal and its smoke. If the land is not appropriate for growing food crops, economic crops can be planted instead. Afforestation is also a promising way for utilisation of the land. Used coal ash and food wastes could be safely used as additions to feeds or fertilizers in low Se area. Based upon the proposed maximum safe level of Se

Conclusion

The imbalance between nutritional need and biologically available amounts of trace elements in the diet comes either from nutritional or from environmental factors. Cereal-dominated, locally produced vegetable diet is an important predisposing factor for many of the endemic diseases, including both trace element deficiency and toxicity caused by the anion group. For prevention, a general supplementation of the specific element to inhabitants rather than to specific populations, is needed, since the geochemical influence is intensive and prevalent. Along with the improvement of dietary habit (increase of animal food, interchange of foods etc.), some endemic diseases could naturally disappear. However, this does not indicate that the specific element intake was met.

Acknowledgement

This author is grateful to W. Mertz and O.A. Levander for their enthusiastic help with literatures.

Reference

1. Underwood EJ, Mertz W Introduction In: Mertz W, ed. Trace elements in Human and animal nutrition. Orlando, Florida: Academic Press, 1986; 2: 1-19.
2. ACC/SCN Preventing anaemia SCN News. 1990; No.6 pp 1-3.
3. Hetzel BS. Progress in the Prevention and Control of iodine deficiency disorder . Lancet 1987; 2: p 266.
4. Levander OA. A global view of human Selenium nutrition, Ann Rev Nutr 1987; 7: 227-250.
5. Kabata-Pendias A, Pendias H. Trace elements in soils and plants. Florida: CRC Press, 1984; pp 51-238.
6. Stiles W. Trace elements in plant (Third ed) Cambridge: University Press, 1961 , pp 59-101.
7. Mengel K, KirKby FA. Principles of plant Nutrition. Switzerland: International Potash Institute Publisher, 1982; pp 473-56.
8. Underwood EJ. Trace elements in human and animal nutrition (Fourth Ed) New York: Academic Press, 1977; pp 258-368.
9. FAO/WHO Expert Consultation. Requirements of vitamin A, iron, folate and vitamin B12. Rome, 1988; pp 11-50.
10. Turnlund JR, Michel MC, Keys WR, *et al.* Copper absorption in elderly men determined by asing stable 65Cu. Am J Clin Nutr 1982; 36: 587-591.
11. Prasad AS. Diagnostic approaches to trace element deficiency. In: Trace elements in nutrition of children-I (Chandra ed) Nestle Nutr. Workshop Series. New York: Raven Press, 1985; 8: 17-31.
12. Arderson RA, Kozlovsky AS. Chromium intake absorption and excretion of subjects consuming self-selected diets. Am J Clin Nutr 1985; 41: 1177-83.
13. Offenbacher Eg, Spencer H, Dowling HI, *et al.* Metabolic chromium balance in man. Am J Clin Nutr 1986; 44: 77-82.
14. Wang WG, Sun SF, Pian LH, *et al.* Relationship between iron status of infants and the methods of feeding. Chinese J Paed. 1991; 29: 212-13.
15. Chen X, Yin T, He J *et al.* Low levels of Zinc in hair and blood, Pica, anorexia, and Poor growth in Chinese preschool children. Am J Clin Nutr 1985; 42: 694-700.
16. Mertz W. Metabolism and metabolic effects of trace elements In: Chandra RJ, ed. Trace elements in nutrition of children - I. New York: Raven Press, Nestle's Nutrition Workshop Series, 1985; 8: 107-119.
17. Mertz W. General consideration regarding requirements and toxicity of trac elements In Trace elements in nutrition of Children — II (Chandra RJ ed.) New York: Vevey press Nestle's Nutrition Workshop series 1991; 23: 1-13.
18. Underwood, EJ. Trace element in human and animal nutrition (Fourth ed.) New York: Academic Press. 1977; pp 271-301.
19. Ma T, Lu T, Tan U, *et al.* The present status of endemic goitre and endemic cretinism in China. Food and Nutrition Bulletin 1982; 4: 13-19.
20. Behne D, Kyriakopulos A, Meinhold H, *et al.* Identification of type 1 indothyronine S - Deiodinase as a Selenoenzyme. Bioch. Biop. Res,

Comm. 1990; 172: 1143-49.

21. Fan W, Li G, Kan D, *et al.* Progress on etiologica studies of KD. Chinese J. Endem. 1989; 8: 52-55.
22. Yu Z, Hu X, Zhu H, *et al.* A study of the relation between iodine and goitre prevalence from insufficient or excessive intake of iodine in humans. Chinese J Endemiol. 1987; 6: 331-34.
23. Wu G, Liu Y, Sun J, *et al.* Survey on The prevailing of endemic fluorosis in China. Chinese J Endemiol 1984; 3: 103-107.
24. Lou X, Hu G, Wei H, *et al.* Effect of molybdenum on etiology, pathogenesis and prevention In Environmental life elements and health (Tan J, Peterson P, Ribang, *et al.* eds) Beijing, Science press. 1990; pp 309-317.
25. Underwood EJ. Trace elements in human and animal nutrition (Fourth ed.) New York: Academy Press, 1977; pp 109-31.
26. Hunt C, Shuler T, Muller L. Concentration of boron and other elements in human foods and personal care products. J Am Diet Assoc 1991; 558-568.
27. Nielsen F. Recent advances in human trace and ultra trace element nutrition. In Abstracts of the 14th International Congress of Nutrition. Seoul, Ewa Womans University 1989; p.61.
28. Newnham R. Tentative evidence of relationships between boron supply and arthritic disorders. In Trace elements in man and animals (Mills, C. *et al.* eds) UK, Common Wealth Agric Buc, 1985; 5: 839-40.
29. Nielsen F. The Ultratrace elements. In Trace Minerals in Foods (Smith K ed) New York: Marcel Dekker, 1985; pp 357-428.
30. Liu H. Endemic arsenic intoxication. In Introduction to Endemiology (Tsou X *et al.* eds) XingJiang, XingJiang people's Publication Agency, 1987; pp 247-278.
31. Yang GQ, Wang GY, Yin TA *et al.* Relationship between the distribution of keshan disease and Selenium status. Acta Nutr Sin 1982; 4: 191-200.
32. Yang GQ. On the etiological relationship of selenium and keshan disease. Adv physiol sciences. 1983; 14: 313-317.
33. Yang G, Ge K. The epidemiology of selenium efficiency in the etiological study of endemic diseases in China (Submit to Am J Clin Nutr 1991).
34. Tan J, Hou S, Zhu W, *et al.* The Keshan disease in China. A study of the geographical epidemiology. Acta Geograph Sin 1979; 34: 85-103.
35. Keshan Disease Research Group. Observation on effect of sodium selenite in prevention of Keshan disease. Chine Med J 1979; 92: 471-476.
36. Chen YY, Qian PT. Observation on The Preventive effect of Se-enriched table salt among 105 million subjects in West China. Chinese J Contr Endem Dis 1989; 4: 50-52.
37. Zhou R, Sun S, Thai F, Yang G, *et al.* The availability of Selenium (1) Selenium Content and glutathione peroxidase activities of blood and tissues of rats. Acta Nutr Sin 1983; 5: 137-144.
38. Ge K, Bai J , Deng X, *et al.* The Protective effects of selenium against viral myocarditis in mice. In Selenium in biology and medicine (G Combs, J Spallholtz, O Levander, J Oldfield eds) New York: Van Nostrand Reinhold Company 1987; pp 761-68.
39. Yang GQ. Research on selenium-related porblems in human health

in China. In Selenium in biology and medicine (G Combs, J Spallboltz, O Levander, J Oldfield eds).New York: Van Nostrand Reinhold Company 1987; pp 9-32.

40. Yang GQ, Yin TA, Liu ST. *et al.* Approaches to the supplementation of selenium for the prevention of keshan disease Acta Nutr Sin 1982; 4: 1-9.
41. Combs G, Combs S. The role of Selenium in Nutrition. New York: Academic Press, 1986; pp 98-121.
42. Yang G. Methods for the prevention of selenium deficiency and toxicity diseases in China. Chinese J Contr Endem Dis 1989; 266-267.
43. Aro A, Alfthan G, Varo P. Se Supplementation of fertilizers has increased the Se intake and serum-Se concentration of Finnish people. In Selenium in biology and medicine (A Wendel ed) Germany, Springer-Verlag, 1989, pp 242-245.
44. Yang GQ, Wng SZ, Zhou Rh, Sun SZ. Endemic selenium intoxication of humans in China. Am J Clin Nutr 1983; 37: 872-881.
45. Sun S, Zhai F, Zhou R, Yang G. Selenium bioavailabilities of soils in KD and seleniferous areas. Chinese J Endemiol 1985; 4: 21-8.
46. Yang GQ, Ge KY, Chen JS, Chen XS. Selenium-related endemic diseases and the daily selenium requirement of humans (Bourne GH ed.). Switzerland: Karger 1988; 55: 99-152.
47. Yin S, Gu H, Zhou R, Yang G. Selenium and associated antagonistic elements content of common foods in Beijing market. Acta Nutr Sin 1986; 8: 27-35.
48. Yang G, Zhou R, Yin S, *et al.* Studies of safe maximal daily dietary selenium intake in a Seleniferous area in China. I, selenium intake and tissue selenium levels of the inhabitants. J Trace Elem Electrolytes Health Dis 1989; 3: 77-87.

Proc 6th ACN 1991: 92-101

Nutrition intervention programmes: success and failure

Kraisid Tontisirin

Institute of Nutrition and Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Thailand

Introduction

Over the last few decades, many nations and concerned international agencies have been working singularly and together to improve the nutritional status of vulnerable population groups, especially young children. The 1960s brought with it the decade of the Applied Nutrition Programme (ANP) wherein various sectors had their own programmes to promote nutrition. Following the ANP, the 1970s called for multisectoral integrated efforts to alleviate malnutrition. Since 1980 and continuing into today, community-based interventions emphasising community participation form the basis for many local and national programmes.

Over this time period, strategies for implementing effective nutrition intervention programmes have long been sought after. These have stressed not only the feasibility of implementation and short-term out-comes, but efforts to promote sustainable nutrition programmes have been of great concern. Although the efforts and outcomes of nutrition improvement programmes have been variable, some countries (such as Indonesia, India and Thailand) have experienced substantial successes. This paper takes a look at the successes, as well as failures, of nutrition intervention programmes in Asia, with an emphasis on protein-energy malnutrition. The discussion focuses on four specific nations (Indonesia, India, Philippines, Thailand) and the lessons learned from their nutrition intervention programme experiences. Special attention is paid towards identifying the crucial elements of successful community nutrition programmes.

Nutrition situation in Asia

Most Asian countries still encounter problems in undernutrition. Protein-energy malnutrition (PEM), iron deficiency, iodine deficiency disorders and vitamin A deficiency are among the most common nutritional problems (1). Infants and young children under five, especially those living in rural poor areas and urban slums, are the most vulnerable groups. In developing countries today, 150 million children under five are seriously malnourished; about 163 million are stunted; and 35 million are wasted (2).

Table 1 shows the prevalence of malnutrition among the underfives in 10 Asian countries where data are available (3). Severe underweight among 0 to 4 year old children is highly prevalent in some countries, such as Bangladesh, Pakistan, Vietnam and Sri Lanka. In other countries, where the prevalence of undernutrition (weight-for-age) is relatively low, chronic

malnutriton (stunning measured by height-for-age) is still prevalent. The magnitudes of stunting among children after two years of age are 20-70%. In addition, other vulnerable groups, namely school children and pregnant women, are also affected.

TABLE 1

Prevalence of underweight (weight-for-age) among 0-4 years children in 10 Asian countries (1980-1987)*

Country	Moderates + Severe	Severe (%)
Bangladesh	60	19
Pakistan	39	10
Laos	37	N.A**
India	41	6
Indonesia	51	1
Myanmar	38	N.A**
vietnam	52	13
Philippines	33	N.A**
Sri Lanka	38	9
Mauritius	24	7

* Reference (3) ** Not Available

Micronutrient deficiencies - especially iron deficiency, iodine deficiency disorders, and vitamin A deficiency — still persist in the region (4). Estimates suggest that 1,300 million people suffer from anaemia, half of them as a result of iron deficiency. The prevalence of iron deficiency anaemia is around 50% among pregnant women and children in many communities of several countries in Asia. Iodine deficiency is also highly prevalent and has been a leading cause of irreversible disorders (i.e., cretinism) despite the long-known cause of the problem. At least 1000 million people who live in iodine deficient environments around the world are at risk for both physical and mental developments. Of these, some 300 million are in China, 200 million in India and 100 million in Indonesia. Vitamin A deficiency remains today as the major cause of preventable blindness in the Third World, although Vitamin A-rich food sources are widely available. Some 13 million preschool children have some degree of xerophthalmia due to severe vitamin A deficiency and some 40 million children go partially or totally blind due to vitamin A deficiency which is a serious public health problem in 37 countries including several countries in Asia.

Unfortunately however, these rates are suspect and, in many cases, probably under-estimate the actual situations. Simple and reliable field methods for assessing these deficiencies as well as a surveillance system to monitor the situations in developing countries have not yet been established. Most notably, there is still no "gold standard" for assessing vitamin A deficiency as a basis for evaluating nutrition programme effectiveness.

In countries which are economically better-off, overnutrition (overweight, obesity) and related diseases are increasing. The incidence and mortality associated with degenerative diseases and their nutritional causes have also increased, especially among urban dwellers.

Nutrition interventions

The most common nutrition interventions are those used to tackle protein-energy malnutrition in young children, notably: (i) growth monitoring, (ii) breast-feeding and supplementary feeding, (iii) nutrition education, and (iv) health services for severe nutritional deficiencies. Interventions for micronutrient deficiencies are highly targeted. Short- to medium-term nutrient-oriented strategies (such as high-dose supplementation and fortification of foods with iron, vitamin A and/or iodine) are employed by several nations

with adequate resources and technical capabilities (e.g., Indonesia, Thailand, Philippines).

Implementation of nutrition interventions as large scale programmes

Presently, nutrition intervention programmes are implemented in one of two ways (or in the case of Thailand, both), either as vertical programmes within a single line ministry (sectoral intervention) or integrative programmes involving several sectors and agencies (multisectoral approach). If effectively implemented, both strategies can produce positive outcomes. Although there is no rule as to which strategy should be used in what situations, the sectoral approach works best when the problem is relatively serious, such as high prevalence of moderate and severe malnutrition. Immediate actions are necessary to prevent death and help ensure child survival. Medium- to long-term programmes generally rest on most intersectoral and horizontal approaches.

Sectoral implementation of nutrition intervention varies. Health sectors generally focus on curative measures where severe and moderate malnutrition cases are referred for treatment of associated infections. During rehabilitation, both preventive and promotive measures (for example, nutrition counselling or proper feeding) may be conducted. The child feeding centre is another form of targeted sectoral nutrition intervention. Supplementary foods are given either as a take-home or on-site feeding to ensure consumption by the intended target children.

In addition, nutrition interventions may be provided through social welfare services to a malnourished child and his/her family. Similar to programmes available through the health sector, food supplements or food rationing is provided to malnourished children (and sometimes their poor families) to ensure actual consumption.

Nutrition education is usually conducted through multi-media channels and various communication strategies. Effective communication is necessary, but it often must compete with mass media (commercial) promotions of nutritionally inadequate food products. This is clearly seen in the promotion of infant formulas and commercially-prepared supplementary foods for infants and young children versus proper infant feeding via breast-feeding and home-prepared supplementary foods. Nutrition education is necessary as both a short- and long-term intervention measure. Usually, the health sector is the responsible agency.

A multisectoral approach, however, comes into consideration when the multi-faceted causes (biological, socio-cultural) of malnutrition are being targeted for change. Theoretically, integrated efforts for tackling such underlying causes appears to be the most effective strategy. In reality though, such an effort is very difficult to implement, and a "top-down" approach is still overwhelmingly used. As will be discussed later, unless the community is involved in all intervention programme stages (problem identification, intervention planning, implementation, monitoring, evaluation), the multisectoral implementation is unlikely to succeed.

Selected nutrition programmes in Asia (1, 5-7)

Asian countries have made substantial efforts in improving the nutritional statuses of their populations. During the past two decades, nutrition programmes in many countries have been successful. To illustrate such efforts in Asia, four programmes are highlighted here — the Family Nutrition Improvement

Programme (UPGK) in Indonesia, the Integrated Child Development Services Scheme (ICDS) in India, the Philippines Nutrition Programme (PNP) and the National Food and Nutrition Programmes in Thailand. The UPGK, PNP and the Thai programmes are community-based interventions entailing political commitment, community resources mobilisation and community participation. The ICDS programme in India differs in that it is the governmental service with a targeting scheme; it also relies on external financial and technical supports.

The UPGK in Indonesia

The UPGK is a nationwide programme supported by the Indonesian government. The UPGK aims at improving the health and nutritional status of the target groups, i.e. children under five years ,pregnant and lactating mothers. Areas possessing the highest mortality rates served as the early intervention sites. Later, the programme was expanded nationwide. The basic programme package includes monthly growth monitoring of the under-fives, health and nutrition education, food demonstrations, home gardening, and nutrition first aid (inclusive of iron and vitamin A supplementation, as well as medical and health services like ORS distribution). Implementation activities have been managed by community leaders and operated by volunteer cadres.

In 1989, reports indicated tht 81-98% of the target child population were weighed. There were positive changes in knowledge and practices along with a relationship between programme attendance and improvements in child weight-for-age. While there was an attempt to involve several sectors in these efforts, the impact was less than expected due to inadequate performance by the health cadres. Cadre performance in nutrition counselling, therefore, needs strengthening through additional training and supervision.

The ICDS Programme in India

The Integrated Child Development Services Scheme was initiated in 1975. The programme is implemented by state governments and receives partial financial support from the central government. Bilateral and international agencies (such as USAID, World Food Programme, and UNICEF) have provided food assistance, equipment and other materials. The programme focuses on providing integrative services for children under five, pregnant and lactating women. The ICDS is implementated through courtyard centers by trained community members and health center staff. Services include on-site and take-home food supplements for children, pregnant and lactating women as well as iron, folate and vitamin A supplements, immunisations, curative care, and health and nutrition education.

An evaluation in 1987-88 showed increased coverage and a substantial reduction of severe malnutrition. The in-service training and close supervision of the community workers improved their technical skills.

The Philippines Nutrition Programmes (PNP)

Since 1974, the Philippine Nutrition Programmes have been implemented through a Presidential Decree, and there has been strong political support for the nutrition activities for almost a decade. The PNP's core activity is growth monitoring for preschool children. Known as the "Operation Timbang", this activity is implemented at the village health station or weighing post in the community. Nutrition volunteers help recruit and weigh the children. Health and nutrition education, family planning services, immunisations and other health services are also provided. As of 1989, village nutri-

tion volunteers covered nearly one-third of all villages in the country. The majority of volunteers were deployed in the most nutritionally-deprived areas.

Due to political instability and nationwide economic setbacks, the PNP's objective of improving the nutritional status of vulnerable groups has not been fully attained. However, progress has been made, and outcomes might have been even worse without the continued efforts of personnel concerned with the nation's nutrition situation. The agency responsible for implementation, specifically the National Nutrition Council, has retained its roles in planning and coordinating nationwide action programmes, despite severe administrative restructuring.

The National Food and Nutrition Programmes in Thailand (7)

Until the mid 1970s , Thailand's nutrition programme was one component of the nation's health plan. Thereafter, the National Food and Nutrition Plan (FNP) was, for the first time, included as an entity in the Fourth National Economic and Social Development Plan (NESDP) (1977-1981). The most significant accomplishment of this plan was the creation of strong awareness about major nutritional problems among the public and private sectors and at all levels. This led to strong political commitments in terms of the country's nutrition policies.

A multisectoral approach was adopted and implemented by four main ministries, namely health, agriculture, education and interior (community development department). Early on however, the nutrition programme was not fully implemented due to a lack of inter- and intra-sectoral collaboration. Further, there was no change in programme planning and the budget allocation structure to support multisectoral efforts. There was also very little participation by the community. Consequently, many of the activities did not achieve their set objectives (for example, centrally produced supplementary food, nutrition rehabilitation in rural villages).When the national nutritional surveillance data first became available at the end of 1982, it showed a strikingly high prevalence of PEM (> 51%) among preschool children (Table 2) . Overall, nutrition programmes employed during the Fourth NESDP were only stopgap measures to relieve the most severe form of malnutrition. Systematically planned long-term solutions were perceived as necessary for sustained improvement of the population's nutritional status.

The Fifth NESDP (1982-1986) continued to include the food and nutrition plan. However, the concept and planning approach changed, because malnutrition was recognised as a manifestation of poverty and ignorance. The main thrust of the Fifth Plan's nutrition policy was thus rooted in the broader policy of poverty alleviation and development of the rural areas. This was the important turning point in the nation's development approach, which formerly focused attention on overall economic growth and its trickle down effects on rural development.

Successful implementation of the community-based nutrition programmes were strengthened and accelerated by the long-term policy to achieve "Health for All by The Year 2000". Two important national policies — rural poverty eradication and primary health care (PHC) — were adopted in the Fifth NESDP. Both policies have nutrition concerns as a main component. The rural poverty alleviation policy focused on identifying poverty areas needing urgent attention. These then served as the target areas for all implementation agencies, including the integration and coordination of activities in rural devel-

TABLE 2

Percent prevalence of protein energy malnutrition (PEM) in preschool children (Wt/Age) Thailand*

Year	No. of children surveyed	Nutritional status (%)			
		Normal	Mild PEM	Moderate PEM	Severe PEM
1982	1,000,000	49.21	35.66	13.00	2.13
1983	1,270,393	64.77	28.5	5.90	0.80
1984	1,590,830	70.67	24.85	4.20	0.27
1985	1,620,518	71.55	24.35	3.90	0.21
1986	2,277,908	74.91	21.84	3.12	0.13
1987	2,351,521	77.11	20.53	2.30	0.06
1988	2,435,129	78.85	19.51	1.60	0.02
1989	2,539,407	79.14	19.72	1.14	0.01

* Division of Nutrition, Ministry of Public Health (7)

opment at central and local levels. There was also a striking organisational change for rural development. One national committee was created (instead of several separate sectoral developmental committees), and it was in charge of development policies and infrastructural development from the central to village levels.

During the Fifth NESDP, the nutrition situation of infants and preschool children improved dramatically. Severe PEM was practically eliminated and only small percent of moderate PEM remained (Table 2). Concerning nutritional assessment, weighing by simple beam balance and use of growth charts by the village-based health volunteers (VHV and VHC, trained under the PHC strategy) and mothers were feasible and useful for problem identification. Simple technology for village level processing of supplementary food was promoted to overcome the disruptive distribution of centrally produced supplementary food. Village self-financing schemes were also attempted with some success.

The concept of "having an improved quality of life" was introduced to replace that of "having good health". The Quality of Life concept was translated into actions via the "basic minimum needs " approach and was implemented as a pilot trial in 1983. In the Sixth NESDP (1987 - 1991), similar strategies continued and the basic minimum needs approach was adopted nationwide to strengthen the integration of sectoral efforts. By 1989, more

than 580,000 village health communicators (VHC) and 62,000 village health volunteers (VHV) were trained, covering almost 100% of rural Thai villages. As a result, the most recent nutritional surveillance report showed that the prevalence of severe malnutrition is almost nil and moderate malnutrition has reduced sharply.

Lessons learned from country experiences

1. Community-based nutrition intervention programmes are more likely to sustain themselves if community resources and manpower are mobilised and community participation is given adequate attention. Local government officers and non-governmental personnel can be facilitators or supervisors (but not dictators) for the community in its attempt to identify its problems and implement practical development solutions.

2. A firm national policy with a well-defined goal for nutrition improvement is crucially important. It is not necessry for it to be a food and nutrition policy. Policies which contain nutrition considerations (such as primary health care and rural poverty eradication as in the Thai case) can be just as effective.

3. There is a need for an effective organisational structure and efficient managerial mechanisms for coordinating and integrating the multisectoral efforts of various administrative levels, especially at district and community levels.

4. It is inadequate to only endorse programmes at the policy level. It is also inadequate to implement segmented, dis-articulated community-based intervention programmes. A "top-down support and coordination" scheme combined with "bottom-up planning and implementation " community approach improves programme implementation and potential sustainability.

5. Continued efforts are required to make honest assessments of how well programmes (national and local) have succeeded. It takes time, maybe 10-15 years or even longer, for changes to be firmly seen in any given indicator (e.g., nutrition status, population growth).

6 The presence of malnutrition does indicate errors in a nation's socio-political, cultural or policy systems. Nutrition intervention programmes cannot be implemented as ready-made, sure-fire programmes. In addition, each strategy (vertical or multisectoral) has advantages and disadvantages. Combined efforts may be necessary to produce desirable impacts. Moreover, due to the dynamism of each country or locality, nutrition interventions should be flexible to suit potential changes.

7. Nutrition can no longer be perceived as only a health or social welfare concern. A population's optimal nutritional status cannot be attained or maintained in isolation of other social and economic development goals, and vice versa. This realisation is very crucial at all levels. An increase in "nutritional literacy" should thus become an integral part of planning nutrition as well as social development programmes.

8. Politicial stability, favourable economic growth, together with explicit policies in food and nutrition contribute significantly to a population's nutrition status improvement. Yet, the Philippines sets a good example in their continued and committed efforts towards nutrition improvement. Despite the economic setback and repeated natural calamities, the nutritional status of vulnerable groups remained at reasonable levels, if not showing improvement altogether.

Crucial elements of successful community nutrition programmes

Lofti and Mason reviewed direct intervention programmes for improving infant and child nutrition (8). Their analysis showed that while direct intervention exerts beneficial effects on child's nutrition, programme successes could be caused by several factors. Well-defined programme objectives, proper intervention choices, strong leadership and efficient management, community mobilisation, adequate training and supervision were among the important features. In their views, direct nutrition interventions are appropriate when food intake is not a constraint, the minimum level of organisational infrastructure exists, and the resources needed are affordable.

Three broad features required for designing nutrition interventions were also defined. First, clear and prioritised objectives must be specified. Second, targeting by areas, age groups, etc. is needed to focus resources. Third, nutrition intervention is inevitably a component of health services since malnutrition and infection are closely related.

Another effort to identify crucial elements for successful nutrition intervention programmes derives from experience of several developing countries (6). Six factors were identified and are briefly discussed here. First, firm and consistent political commitments to support concrete nutrition financing and action are crucial. Political commitment can be elicited through advocacy by professionals or international agencies as well as communities needing programmes.

Second, effective community mobilisation is crucial. It is based on involving community members in all development stages — from needs assessment, programme planning, implementation and monitoring and evaluation. Decentralisation of decision-making to the lowest possible level and empowering the community to deal with their own problems can generate high levels of community participation.

Third, human resources development — most notably skills-oriented and competence-based comprehensive, multidisciplinary training — was recommended. However, a relatively large investment is required for basic and in-service training. Fourth, appropriate targeting improves the efficiency and cost-effectiveness of nutrition intervention programmes. Fifth, a functional management information system is crucial for programme monitoring and decision-making at all levels. Sixth, two interrelated elements, namely, replicability and sustainability were identified.

To take another step further, successful implementation of nutrition programmes does not lie in identifying the crucial elements. In practice, introducing the right element(s) at the right time, given existing situations and opportunities, is even more crucial. Using food and nutrition data/information to create the "right" awareness at all levels is critical to gain political commitment and suspports. Social mobilisation and a nation's favourable organisational structure for implementating community-based programmes are essential for sustainable efforts.

Conclusion

Nutrition intervention efforts have been implemented as large-scale programmes in several developing countries in Asia. The progress made is impressive, especially in the short-term where malnutrition alleviation has been directed towards high risk or specific target groups. The strategies employed, however, tended to be stopgap measures aimed at improving the survival of especially vulnerable groups (primarily infants and young children).

Direct interventions have been the customary mainstream efforts, both sectoral and multisectoral. Some

programmes demonstrating present success have the potential to be sustainable in the long-run, but only if active community participation is encouraged in undertaking these interventions.

Explicit policies in food and nutrition, as a self-contained policy or a component of broader development policies, are needed to strengthen and facilitate nutrition improvement efforts. Political stability and commitment, economic growth and organisational structure are favourable factors for successful large-scale nutrition programmes.

Final remarks

Experiences in Asia during the past decade have significant progress in nutrition improvement. The question of sustainability however remains to be seen, especially for sectoral programmes. Programmes which address only single aspects of malnutrition's complex chain are less likely to be sustained, since the causes of malnutrition are complex.

Food security at national, household and individual levels assures the availability of foods. To achieve food security, food production activities — not only of staples, but also other nutritious food items — must be promoted. Greater understanding of needs for the right kinds of food oftentimes determines food intakes. Therefore, nutrition education and dietary guidelines for each population group are necessry elements in the nutrition intervention.

In subsistence communities, local food production and food gathering from natural sources are important means of food acquisition. Where food is commercialised, consumer protection both by laws and mass campaigns for proper diets and safe foods are important. In countries or communities which are transitioning into a market-based economy, increasing purchasing power via income generation activities or indirect intervention must be considered. Thus, the roles of agriculture, education and other development sectors are obvious.

In addition, closely linked with proper nutrition is illness, especially infections. This calls for effective preventive and promotive health measures along with nutrition programmes. Holistic thinking and its translation into plans of actions should remain the approach used in the coming decades.

To make these integrative efforts possible, nutritionists and other related personnel must understand the nature of nutritional problems and have access to information system which provides proper and timely information. Food and nutrition surveillance will allow for monitoring of the situation, especially among vulnerable groups. In the long-term, nutrition for all age groups should be addressed nationally. Thus, an effective management information system along with improvements in nutritional literacy should be high priorities in national policies and plans. Nutritionists can play important roles in both planning and research for development. Human resources development is necessary at all levels, and especially among policy-makers, country managers, trainers, researchers and community-level workers.

Comparatively, Asian nations demonstrate a broad spectrum in terms of their nutrition situations. There are countries which still struggle to insure child survival; some are working towards full potential in child growth and development ; and a few countries, namely, Japan and Korea, have already reached the stage of high potential in child growth and development. Nutrition intervention programmes in this region, therefore, have a wide range — from child survival, to undernutrition, to overnu-

trition. Member countries should identify mechanisms by which experiences and knowledge learned from several impressive programmes can be exchanged and collaborative training and research efforts developed. These experiences will be beneficial to the Asian Region as well as other parts of the world.

Acknowledgement

The author thanks Dr Pattanee Winichagoon for her efficient assistance in preparing this paper and Mr George A. Attig for final preparation of the manuscript.

References

1. Gopalan C. Nutrition Problems and Programmes in South-East Asia. New Delhi: WHO Regional Office for South-East Asia, 1987.
2. Carlson B and Wardlaw T. An Assessment of Child Malnutrition. New York: UNICEF, 1990.
3. UNICEF. State of the World's Children. New York: UNICEF, 1990.
4. FAO/WHO Framework Paper. Meeting the Nutrition Challenge. Rome: FAO/WHO Joint Secretariat for International Conference on Nutrition, 1990.
5. Tontisirin K. The nutrition situation and nutrition action programmes in four ASEAN countries. ASEAN Fd J 1985; 1: 162-168.
6. International Nutrition Planners Forum. Crucial elements of successful community nutrition programmes, Report of the Fifth International Conference of the International Nutrition Planners Forum, sponsored by USAID, Seoul, Korea, August 15-18, 1989.
7. Tontisirin K and Kirananda T. Public policy and implementation strategies for alleviation of malnutrition and poverty in Thailand. Presented at the meeting on "the Financing of social services during the 1980's and policy options for next decade". Florence: UNICEF Office, March 1-3, 1990.
8. Lofti M and Mason J. Direct intervention programmes to improve infant and child nutrition, (draft), 1990.

Proc 6th ACN 1991: 102-105

Developments in nutritional research methodologies-goals, challenges and accomplishments

Venkatesh Iyengar

International Human Nutrition Programme, NIST, Building 235, B125, Gaithersburg, Md 20899, U.S.A.

Introduction

A reliable nutritional assessment for public health purposes is a globally sought goal by a large number of investigations. The methods used to achieve this goal are classified under (a) dietary studies, (b) anthropometric measurements and (c) laboratory investigations. In practice, there are many challenges involved in using these methods meaningfully since studies related to population groups are difficult to design; factors such as the ageing process, genetic diversity and environmental influences and related statistical considerations are not always easy to comprehend. Furthermore, the need for applying several methodologies, probable inappropriate use of such procedures, and a lack of reliable reference data in some cases signal additional problems to be anticipated. To overcome these difficulties, it is necessary to adopt interdisciplinary approaches. Failure to do so can under worst circumstances, totally nullify the results. Thus, the achievements here are also a measure of success of the multidisciplinary approach to the problem. In this communication, the intricacies in planning dietary assessment studies, and emerging trends related to analytical strategies, development of multipurpose reference materials and nutrition labelling, are exemplified.

Intricacies in dietary assessment studies

Dietary assessment studies basically fall into 3 modes: direct analysis of diets, computation from records (from dietary) components used in conjunction with food composition tables) and biological monitors (for selected constituents).

Direct analysis refers to chemical assays performed on duplicate portions of meals, simulated meals prepared in a laboratory, total diets consisting of a market basket of foods reflecting a defined total diet of consumers, and investigations of individual foodstuffs. A limitation of this approach is that sample sizes involved in these investigations are usually small. Also, there are probable sources of errors arising from sampling (reflecting true intakes, weighing, homogeneity and contamination during collection, preparation). The most affected constituents are trace elements (during sampling and sample handling) and organic nutrients (due to processing and storage conditions which may alter the content of vitamin A, vitamin C and folic acid, among others). The problem with trace elements demands strict control of working procedures and equipments to minimize extraneous contamination. The organic nutrients require either some pretreatments or individual attention in assaying constituents that are sensitive to processing.

Nutritional assessments from food composition tables are applicable to large scale studies, e.g. food consumption at the national level by food balance sheets. The modes applicable to individual consumption are, the 24-hour recall method, repeated recalls over several days, and the estimation from food records. However, the scientific merit of the information depends upon the reliability of the database. Importantly, it should be recognised that the recorded compositions are at best average concentrations for a particular type of food. Besides, incorrect description or the coding errors of food items and nutrients, and whether the results represent cooked foods or not, may introduce random errors. Systematic errors should also be anticipated for trace elements (e.g. a positive bias due to contamination of elements such as Cr, and a negative bias due to volatilisation of Hg and B, among others) and for organic nutrients (e.g. both positive and negative errors due to loss of vitamins and methodological problems with microbiological assays).

Biological monitors such as urine are valid only for selected constituents such as sodium and among trace elements mainly for B, F, Br and I, which are predominantly excreted through this medium. Hair has some applications which are restricted to monitoring toxic entities such as As and methyl mercury.

Irrespective of whether the direct or the indirect analysis approach is chosen, it should be recognised that these evaluations represent the maximum amounts of nutrients available to the body, and that the bioavailability factor is not taken into consideration. Therefore, the nutritional assessment process is incomplete since the influence of parameters such as phytate, fibre and Ca is unaccounted. Similarly, age factors and nutrient sources may interfere with the nutritional assessment status for some organic nutrients. For example, adequate intake of beta-carotene through foods may not necessarily signal adequacy of vitamin A status since absorption of beta-carotene varies in different kinds of foods, and its conversion to vitmain A decreases with age. As for the superiority of one method over the other, both methods have some merits. While the direct method is frequently used where trace elements are involved, the indirect method is a valuable approach especially for large scale studies when the food composition tables are upgraded with reliable data on trace elements.

Analytical strategies for large scale studies

When several countries or several laboratories in the same country are involved in a study, it is not uncommon to find the results for a given element being generated by several methods. This approach should not pose any problems provided that the analytical performance of each method for the analyte of interest is established by analysis of suitable reference materials (RM) (1). For example, this has been effectively demonstrated in a study of Cd and Pb in human whole blood (2). However, only a limited number of studies has been successful using this approach since it requires well coordinated efforts to incorporate all the precautions into the study design and effectively monitor the analytical performance of participating laboratories. This fact is further substantiated by the discrepancies reported for intercomparison runs of RMs (1). An alternate approach to this problem has been attempted in recent studies investigating the composition of breast milk (3) and in an on-going dietary investigation (4). In this approach, each element was determined by only one reference laboratory using the most suitable technique (evaluation based on suitability and performance) to elimi-

nate interlaboratory differences. The quality of the data reported by that laboratory was checked by means of suitable reference materials, by blind analysis of RMs, and also by occasionally checking split-samples by a second method. This approach has worked efficiently requiring minimum centralised supervision of analytical performance.

Multipurpose biological reference materials

Ensuring adequate quality control (QC) of analytical measurements including both inorganic and organic constituents (and speciated analytes e.g. methyl mercury and arsenobetaine) in dietary investigations demands several considerations. Recently developed analytical standard reference materials (SRM) such as non-fat milk powder (NIST-SRM-1549), cow milk powder (IAEA-CRM-A-11), wheat flour (NIST-SRM-1567a), rice flour (NIST-SRM-1568a), bovine serum (NIST-RM-8419), and mixed diet (IAEA-CRM-H9) have gone a long way in meeting the needs of inorganic analysis. Similarly, on the organic side, the coconut oil standard (NIST-SRM-1563) is certified for fat soluble vitamins and cholesterol. Further, for specific constituents such as cholesterol, a range of materials such as NIST-SRM-911b (pure cholesterol) and NIST-SRM-1845 (whole egg powder for high cholesterol content standard), are available. Similarly, the European Community Bureau of Reference (BCR, Belgium) has produced single cell proteins, soya-maize oil and animal fat preparations for fatty acid profile. The need for both kinds of standards has been recognized by the analytical and nutritional communities, and search is underway to identify representative matrices as multipurpose standard reference materials (SRM) for both organic and inorganic constitutents. As a potential solution to this problem, the suitablility of a total mixed human diet as a common analytical reference matrix for both organic and inorganic constituents has been explored. Thus, the total diet standard NIST-SRM-1548 certified for total fat, Kjeldhal N for protein, dietary fibre, cholesterol, caloric content and minerals (5).

Multipurpose SRMs are difficult to develop, yet they play a pivotal role in proper use of RMs. Their impact may be envisaged in a 4-stage process: 1. Preparation of a few carefully chosen matrices that are representative of natural concentration levels of nutrient; toxicant and environmental-indicator elements on the inorganic side, and proximates, vitamins, pesticides and other harmful compounds on the organic side, and certified for as many constitutents as possible. Such a material would satisfy the QC requirements for measurements at natural concentration levels. 2. Identification and preparation of special materials that are naturally enriched in specific constituents, for example, oyster for Zn, fish for methyl mercury, kidney for Cd, egg powder for cholesterol and specific organic matrices for biphenyls etc, for meeting special needs. 3. Preparation of deliberately spiked materials for occupational health problems (e.g. blood and urine spiked with As and Pb) and for monitoring foods fortified with specific nutrients (e.g. infant formula). 4. Use of spiked standard matrices for testing the performance of less sophisticated analytical techniques to explore their suitability for monitoring fortified foods as required by some nutrition labelling programs discussed below.

Nutrition labelling, implementation and requirements

There is a growing public desire to understand the nutrient profiles of foods consumed. As a result, several countries are now enacting laws to make nutrition labelling obligatory. In principle, nutrition labelling is an

extension of the strict labelling requirements mandatory for weaning foods. Similarly, general guidelines are emerging in support of analytical requirements for a broadly based labelling process (6). Foods with (fortified) and without (natural) fortification are subject to different labelling criteria. Constituents such as calories (and fraction attributable to the total fat content), total fat (and saturated fatty acids and cholesterol), carbohydrates, protein, total dietary fiber, selected vitamins (e.g. A, C and D) and minerals (e.g. Na, Ca and Fe) are required to be labelled. Additional nutrients may be added to the label depending upon the product claim. Crucial for implementing nutrition labelling is an understanding of the methodological implications used to assay the label contents and the availability of suitable RMs to validate the measurements. As discussed in the previous section, several food RMs certified for constituents of interest for nutrition labelling are already available. While a number of these are certified mainly for inorganic analytes, NIST-SRM-1548 Total Diet is relevant to nutritional labelling requirements.

References

1. Iyengar GV. Elemental Analysis of Biological Systems, Volume 1: Biomedical, Environmental, Compositional and Methodological Aspects of Trace Elements. 1989, CRC Press, Boca Raton, FL.
2. Friberg L, Vahter M. Assessment of exposure to Pb and Cd through biological monitoring: Results of a UNEP/WHO global study. Environ Res 1983; 30: 95-128.
3. Parr RM, DeMaeyer EM, Iyengar GV, *et al.* Minor and trace elements in human milk from Guatemala, Nigeria, Philippines, Sweden and Hungary: Results from a WHO/IAEA Joint Project. Biol Trace Elem Res 1991; 29: 51-75.
4. Coordinated Project on Human Daily Dietary Intake of Minor and Trace Elements (on-going project). 1991, IAEA (Dr. R.M. Parr), Vienna, Austria.
5. Wolf WR, Iyengar GV, Tanner JT. Mixed diet reference materials for nutrient analysis of foods: Preparation of SRM- 1548 Total Diet. Z Anal Chem 1990; 326: 696-700.
6. Codex Alimentarius Commission. Report of the 19th Session of the Codex Committee on Food Labelling, March 1987, Ottawa, Canada.

Proc 6th ACN 1991: 106-109

A critical assessment of dietary sampling techniques for the determination of trace nutrients

[1]Mohamed Abdulla, [2]Robert M Parr and [3]Fatima Reis

[1]Faculty of Medicine, Hamdard University, New Delhi, India; [2]Division of Life Sciences, International Atomic Energy Agency, Vienna, Austria; [3]LNETIDEEN, 2685 Sacavem, Portugal

Introduction

One of the basic requirements for nutrition research concerned with trace nutrients is the knowledge of the exposure levels. From a public health point of view, it is important to assure the general population that the intake of all nutrients, including the micronutrients, is adequate in the average, normal daily diet. At the same time, the ideal diet should not contain more than the permitted levels of toxic components. Information concerning the dietary intake of essential trace nutrients including the trace elements from prepared meals is very limited at this time. The concentration of some of these trace nutrients in the human body is very low and it is generally believed that a pure nutritional deficiency of these nutrients rarely occurs in man. On the other hand, the adequacy of a modern all-round diet as regards trace nutrients is presently being debated. Marginal deficiency of several trace nutrients, including trace elements and vitamins have been shown to exist in parts of the populations of both industrialised and developing countries (1-3).

Since there are no suitable techniques for the diagnosis of marginal deficiencies of trace nutrients, it is crucial to know the true intake levels from prepared meals in order to deal with such deficiencies. During the last couple of decades, public health authorities in many different parts of the world have started to take an interest in defining desirable levels of nutrient intakes for their populations (4). Some of these efforts have also been duplicated at the international level by bodies such as the World Health Organisation (WHO) and the Food and Agricultural Organisation (FAO) (5, 6).

Methods for the assessment of trace nutrient intakes

Information on daily dietary intake of trace nutrients by individuals or groups can be obtained by:

(a) Direct methods

(b) Indirect methods

(c) Estimation from biological markers

Direct methods

Only the direct analysis of actual food consumed during 24 hours can provide an accurate estimate of the dietary intake of trace nutrients. The methods that are currently used for the assessment of daily trace nutrient intakes are:

(1) The precise weighing of actual food consumed during 24 hours

(2) The duplicate portion sample collection technique

(3) Market basket or total diet studies

The precise weighing technique

Theoretically, the most accurate technique for the assessment of daily dietary intake of trace nutrients is by the weighing and the subsequent analysis of the replicate portions. The investigator can either analyse each meal (e.g. breakfast, lunch, snacks etc.) or analyse the whole sample collected during the 24 hours. The weighing technique works best when it is possible to weigh each component as it is put on the plate and, when possible, to weigh and deduct leftovers at the end of all meals consumed during the test period. Although very accurate, this technique is time-consuming and is a difficult job for the individual participant. The presence of the investigator may also influence the normal dietary pattern.

Duplicate diets/duplicate portion technique

The duplicate diet is a copy (based on visual judgement) collected while eating to represent the foods and fluids normally consumed during a 24-hour period. This method relies on sound background work from nutritionists in the field to ensure the dietary collections are accurately performed.

Although slightly inferior to the actual weighing technique, the duplicate portion sampling technique is probably the most satisfactory and practical procedure for estimating the daily dietary intake of trace nutrients in small well-defined population. The validity of this technique can be investigated independently by checking urine nitrogen, sodium and potassium with and without simultaneous analysis of duplicate portions for the same analytes (7-10). When the study population is well-defined and properly supervised, underestimation can be reduced to as little as 5-10% (11). Underestimation becomes more significant when the collection period exceed 24 hours.

Market basket/total diet studies

The principle behind this technique is that a typical diet for a particular country, area or group is constructed and the foods are purchased and prepared for consumption prior to analysis. The construction of the diet is often based on household purchase or disappearance data for the population. This method does not assess the variability of intake of individuals or expose intake extremes.

Indirect methods

Indirect methods are based on computation from standard food tables. For the study of all major nutrients including trace nutrients in large population groups, computation from standard food tables remains the method of choice. Most methods rely on tables containing values for cooked foods, which may themselves be calculated from the analysed raw food table. The following is a list of the most commonly used methods for obtaining data on food consumption:

(1) Food balance sheets; per capita consumption

(2) Household food surveys

(3) 24-hour and 7-day recalls

(4) Diet histories and frequency questionnaires

(5) Unweighed records; dietary dairies

(6) Weighed intake studies

Generally speaking, all methods mentioned above have limitations. The concentration of many trace nutrients in food are low and the data for some of them may not be available in food tables. This is specially the case in the food tables of many developing coun-

tries. Values described as 'unavailable' are often accepted as negligible leading to a negative bias. Systematic errors also arise as food tables are only appropriate for the country in which they are compiled but are sometimes used in other countries. Inconsistencies between different food tables appear due to differences in sampling procedures, analytical methodology or factors employed to convert analysed values to nutrients. Comparison of results of dietary surveys using different food tables are therefore open to bias. Data from food balance sheets, and household surveys are only useful as a guide to average population intakes. Unweighed dietary studies conducted on large sample numbers may have some value, and weighed studies are of value in determining intakes of individuals and small population groups.

Estimation of intakes from biological markers

The most commonly used biological materials for the estimation of trace nutrient intake levels are urine, faeces, whole blood/plasma/serum, hair, nails and sometimes specific cell lines such as neutrophils. For certain trace nutrients such as iodine and selenium, urinary excretion reflects intake levels when corrections are made for the losses through skin, lungs and faeces. The main excretory route for many trace nutrients is via faeces and it is possible to calculate intake levels by faecal excretion. Due to obvious practical problems in monitoring faecal excretion, intakes are seldom calculated from the excretion in faeces. Whole blood/plasma/serum levels of trace nutrients are poor indicators of current intake levels due to their fluctuations independent of intake levels. At the present time, there is no universal agreement about the use of hair, nail and cell lines as predictor of body status including the intake levels of trace nutrients. Hair analysis in combination with blood analysis can be useful in some cases, especially with regards to certain toxic metals such as mercury and arsenic.

Table 1 shows the source of errors in the commonly used techniques for estimating trace nutrient intakes.

TABLE 1
Sources of error in the commonly used dietary sampling techniques

Sources of error	Techniques		
	Direct Methods	Indirect Methods	Biological Markers
Addition and omission of foods	no	yes	no
Amount and frequency of foods	no	yes	no
Day to day variation and changes in dietary pattern	yes	no	no
Sampling and analytical errors	yes	no	no
Food composition table errors	no	yes	no

Conclusion

It can be stated that most methods have limitations in their capabilities for estimating trace nutrient intakes. In order to make valid intake estimates, one should use a combination of methods. As long as one is aware of the limitations of each method, it is still possible to make use of the current literature concerning dietary intakes for comparison and recommendation purposes.

References

1. Abdulla M. Inorganic chemical elements in prepared meals in Sweden. University of Lund, Sweden, Ph.D Dissertation, 1986, pp. 90-8.
2. Mertz W. Some aspects of nutritional trace element research. Fed Proc 1970; 29: 1483-8.
3. Mertz W. The essential trace elements. Science 1981; 213: 1332-8.
4. IUNS. International Union of Nutritional Sciences, Report of Committee 1/5, Recommended dietary intakes around the world. Nutrition abstracts and reviews in clinical nutrition - 1983; A 53/11: 939-1015.
5. WHO. Handbook of human nutritional requirements. WHO monograph series No. 61, 1974, WHO, Geneva.
6. FAO. Requirements of vitamin A, iron, folate and vitamin B12. FAO food and nutrition series No. 23, Food and Agriculture Organizaiton, Rome, 1988.
7. Abdulla M, Andersson I, Asp N-G, *et al.* Nutrient intake and health status of vegans. Chemical analysis of diets using the duplicate portion technique. Am J Clin Nutr 1981; 34: 2464-77.
8. Abdulla M, Aly K-A, Andersson I, *et al.* Nutrient intake and health status of lactovegetarians: Chemical analysis of diets using duplicate portion sampling technique. Am J Clin Nutr 1984; 40: 325-38.
9. Isaksson B. Urinary nitrogen output as a validity test in dietary surveys. Am J Clin Nutr 1980; 33: 4-12.

Proc 6th ACN 1991: 110-113

Bioavailability of inorganic nutrients - speciation chemistry and recommended dietary intakes

Ivor E Dreosti

CSIRO Division of Human Nutrition, Adelaide, South Australia

Introduction

Interest in the bioavailability of trace elements from human diets has recently gathered momentum following accumulating evidence that differences in nutrient absorption and utilisation impact materially on the precision of estimates of the Recommended Dietary Intakes (RDIs) for several micro-elements. Over the last decade scientists from widely differing research disciplines have examined the question from a variety of viewpoints. Physico-chemists, for example, have studied factors in food which affect the availability of trace elements for absorption from the gut lumen, due to their influence on the solubility of elements in the intestinal milieu or because they lead to trace element chelation or competition between ions for binding by mucosal uptake mechanisms.

Physiologists in turn have focussed their interest on metabolic factors which may affect the uptake of trace elements from the gastro-intestinal tract, for example, age, the prevailing micro-element status or the saturation kinetics of carrier uptake mechanisms, as well as those physiological conditions and nutritional interactions which might influence the bioutilisation of trace elements already absorbed and present in the cellular environment.

Bioavailability

Physiological factors which affect bioutilisation, and which may significantly influence the overall bioavailability of some nutrients, are often overlooked because of a tendency for investigators to focus primarily on those physico-chemical influences in the gut digesta which specifically affect nutrient absorption. However, by definition, bioavailability refers to the proportion of a nutrient in food which is absorbed and ultimately utilised within the tissues, which places emphasis equally on both physiological and physico-chemical factors (1). For several trace elements the utilisation component of bioavailability can be of considerable importance, for example, selenium ingested as inorganic selenate/selenide is treated differently from seleno-methionine and has to be reduced before it can be incorporated into the seleno-cysteine of seleno-proteins (2). The effective utilisation of iron for haemoglobin synthesis depends critically on an adequate level of copper-containing ceruloplasmin (3), while the level of the thyroid hormone trio-iodothyronine is strongly influenced by the activity of a selenium-dependent T_4-deiodinase enzyme (4).

Generally, however, and in a purely dietary setting, most attention has logically centred on the many physico-chemical factors which affect trace element absorption, and thereby influence the bioavailability and subsequent estimates of RDI. To the nutritionist, these are issues which can be addressed and to some extent evalu-

ated by examination of the diets in question in relation to their trace element speciation and association with organic macromolecules.

Physico-chemical factors affecting bioavailability

Solubility

Absorption of trace elements from the gut hinges centrally on aqueous transport mechanisms, with the result that water solubility represents a key factor underlying the efficiency of the overall process. Accordingly, chemical forms of trace elements which tend to be insoluble under conditions prevailing in the gastro-intestinal tract (eg. some oxides, silicates, sulphides, phosphates) are, for all practical purposes unavailable, while compounds exhibiting increased water solubility (eg. chlorides, sulphates) are almost always accompanied by enhanced intestinal uptake.

Chelating agents

Factors in food which decrease the solubility of an element by chelation (eg. phytate, tannins) reduce bioavailability and increase the RDI estimate. Food components which compete with antagonistic chelators and maintain water solubility (eg. zinc-amino acid chelates versus zinc-phytate) improve bioavailability and reduce the estimated RDI.

Competition for uptake mechanisms

Absorption of trace elements from the intestinal lumen generally involves both passive and carrier mediated mechanisms, which may or may not be energy-linked. Antagonism between elemental ions for transport carrier molecules can markedly reduce bioavailability, which highlights the need to ensure an optimal trace element balance in the diet between potentially competing ions. Competition between ions can be broadly predicted from their electronic configuration when chelated, and from their calculated co-ordination number. On this basis, competition would be expected between Zn^{++}, Cu^{+} and Cd^{++}, all of which exhibit a co-ordination number of 4 and a sp^3 tetrahedral chelate configuration. By contrast, Ca^{++} (co-ordination number 6, chelate configuration $d^2 sp^3$ would not be expected to compete (5). Further modification of the competitive interaction between ions occurs in relation to the affinity constant exhibited by the carrier receptor protein for a particular cation, which can vary substantially (6).

Bioavailability and recommended dietary intakes

To the nutritional scientist concerned with the precise estimation of trace element RDIs, issues relating to differences in bioavailability between diets pose a vexing problem. Of the 5 or 6 trace elements for which RDIs have been set, iron and zinc best reflect the problem and the way in which workers in the area are currently attempting to resolve the question within a practical framework.

Iron

Several factors affect iron absorption favourably, while others depress it. In the former category, iron incorporated into the heme molecule must rank as the principal determinant for good iron absorption. The mechanism for heme iron absorption is quite separate from that of inorganic iron, and involves the uptake of heme by gut mucosal cells and the release of iron intracellularly by enzyme action (3, 7). Animal protein also enhances iron uptake independent of the heme-iron

effect, but whether this is due to the provision of amino acids which form well absorbed, water soluble iron-amino acid chelates is debateable (3). In addition, reducing agents in the diet such as ascorbic acid act to enhance iron absorption by maintaining free iron as the ferrous iron, in which form it is most readily transported into the gut epithelium (3). By contrast, iron chelated by plant polyphenols (eg. tannins) or by phytate is rendered very much less soluble and is considerably less bioavailable (3,8,9).

Because of the many factors influencing iron bioavailability no single RDI for iron is appropriate, and current practice instead presents several estimates for each age/gender category, ranging from a low bioavailability (5-10%) and correspondingly higher RDI for people consuming a predominantly vegetarian diet, to a lower RDI for communities ingesting mixed diets with relatively high intakes of heme iron and animal protein, for whom the bioavailability is adjudged to be in the region of 20% (3, 10, 11).

Zinc

Similar, but different, problems exist in relation to zinc absorption as occur with iron. Thus, vegetarian diets, which tend to be low in zinc content, are further compromised by poor availability of the element due to chelation with phytate, fibre, and to a lesser extent some of the poorly digestible forms of plant protein (12). Dietary enhancers of zinc absorption are less effective than those associated with iron nutriture and tend to involve mainly chelation with certain favourable amino acids or small carrier molecules like citrate (12, 13). Nevertheless, the overall effect on setting a zinc RDI is the same as that for iron, with the result that while some committees setting national RDIs have stressed the restricted availability of zinc from vegetarian diets (10, 14), the WHO Expert Committee on Trace Elements in Human Nutrition (15) and the WHO/FAO/IAEA Expert Consultation on Trace Element Requirements in Humans (16) present several levels of recommended zinc intakes depending on the bioavailability of zinc in the diet, which ranges from an estimated 10% for vegetarian-type diets to 40% from a mixed western diet.

Conclusions

The nutritional bioavailability of dietary trace elements can be significantly affected by their chemical speciation and their association with organic macromolecules. An understanding of these effects is essential if meaningful estimates are to be made of RDIs for population groups with substantially different dietary profiles.

References

1. O'Dell BL. Bioavailability of trace elements. Nutr Rev 1984; 42:301-6.
2. Levander OA. Selenium. In: Mertz W, ed. Trace elements in human and animal nutrition, 5th ed. New York: Academic Press, 1989: 209-80.
3. Roeser HP. Iron. J Food Nutr 1986; 42:82-92.
4. Arthur JR, Beckett GJ. The roles of selenium in thyroid hormone metabolism. In:Momcilovic B, ed. Trace element metabolism in man and animals, Vol 7, Proceedings, 1991:in press.
5. Hill CH, Matrone G. Chemical parameters in the study of in vivo and in vitro interaction of transition elements. Fed Proc 1970; 29: 1474-88.
6. Williams RJP. Zinc: What is its role in biology? Endeavour 1984; 8: 65-70.

7. Turnbull A. Iron absorption. In: Jacobs A, Worwood M, eds. Iron in biochemistry and medicine. London: Academic Press, 1974: 369-81.

8. Graf E, Eaton JW. Antioxidant fractions of phytic acid. Free Radical Biol Med 1990; 8: 61-9.

9. Torrance JC, Gillooly M, Mills W, *et al.* Vegetable polyphenols in iron absorption. In: Saltman P, Hegenaner J, eds. The biochemistry and physiology of iron. New York: Elsevier, 1982:819-35.

10. National Health and Medical Research Council. Dietary allowances for use in Australia. Canberra: Australian Government Publishing Service, 1991:in press.

11. Joint FAO/WHO Expert Consultation. Requirements of vitamin A, iron, folate and vitamin B_{12}. Rome:FAO, 1988:33-50.

12. Sandstrom B, Lonnerdal B. Promotions and antagonists of zinc absorption. In: Mills CF, ed. Zinc in human biology. London: Springer-Verlag, 1989:57-78.

13. Bremner I, Mills CF. Absorption, transport and tissue storage of essential elements. Phil Trans R Soc Lond 1981; B294:75- 89.

14. Food and Nutrition Board. Recommended dietary allowances, 9th ed. Washington DC: Nat Acad Sci, 1973:144-7.

15. WHO Expert Committee. Trace elements in human nutrition. Geneva WHO, 1973:9-14.

16. Joint WHO/FAO/IAEA Expert Consultation. Trace element requirement in humans. Geneva:WHO.

Proc 6th ACN 1991: 114-116

Application of stable isotopes in human nutrition research in developing countries

[1]PS Shetty and [2]MN Ismail

[1]Nutrition Research Centre, Department of Physiology, St. John's Medical College, Bangalore, India; [2]Department of Food Science and Nutrition, Universiti Kebangsaan Malaysia, Malaysia

Introduction

Several important areas of human nutrition in developing countries need to be addressed on a priority basis. These include questions related to energy and protein requirements of normal populations in these regions as well as the vulnerable groups within them, chiefly women and children. Questions related to increase in requirements with frequent infections and for catch-up growth during recovery from infection need to be answered. Quantification of losses that occur during periods of infection, in particular gastrointestinal losses, are also essential. Much of the lacunae in our understanding of these problems specific to poor countries of the Third World need to be tackled on an urgent basis by initiating studies using newly emerging tools such as stable isotopes.

Isotopes of an element have nearly identical chemical behaviour but different physical properties. Isotopes are either stable or radioactive. Radioactive isotopes disintegrate spontaneously at specific rates and emit radiation in the process. They are hence potentially harmful to living organisms but are easy to detect and use. Stable isotopes are safe because they emit no external measurable radiation and are hence considered as silent tracers. The absence of risks of radiation make stable isotopes safe for pregnant and lactating women as well as for studies on newborns, infants and children. But stable isotopic tracers are more complicated to estimate and their presence in excess of natural levels is detected only by changes in the ratio of minor isotope to major isotope.

Both stable and radioactive isotopes have been used in human metabolic and nutrition research. The use of stable isotopes in biological and human research is not a new phenomenon and has occurred in parallel with the development of sensitive instruments to detect them in biological fluids and tissues. Ashton invented the mass spectrograph which was superceded by Mass Spectrometers to estimate quantitatively the relative abundances of the isotopes. The Mass spectrometry systems of the present day are sophisticated, user friendly systems which are becoming increasingly popular being less expensive and hence enhancing the cost-benefit ratio of the use of stable isotopic tracers in human metabolic and nutritional research. The great appeal of stable isotopic tracers however is that they can be administered to human subjects orally and the metabolic products into which they enter can be sampled in breath, saliva, milk, urine or faeces. Thus stable isotopic tracers are silent, safe and use non-invasive sampling procedures thereby simplifying the

conduct of field studies in developing countries. Four major stable isotopes have been extensively used in nutrition research and they are Deuterium, ^{18}Oxygen,^{15}Nitrogen and ^{13}Carbon.

Doubly-labelled water technique

The recent, explosive interest in the use of stable isotopic tracers for nutritional research can largely be attributed to two parallel developments. The first was the recommendation of the FAO/WHO/UNU Expert Consultation (1) to rely on measures of energy expenditure rather than dietary intakes to arrive at energy requirements of populations worldwide. The second, has been the contribution of doubly-labelled water (DLW) technique to measure energy expenditure in free living animals using a combination of stable isotopes of deuterium and ^{18}Oxygen (2). When DLW is administered to a subject both isotopes mix with the body water and are eliminated in the body fluids over a period of days. Since ^{18}Oxygen is also incorporated into exhaled CO_2, the turnover of the two isotopes are different and this difference provides an estimate of CO_2 production rate which can be used to calculate the total energy expenditure. DLW provides cummulative measures of total energy expenditure over a period of weeks in free living individuals but does not provide data on the various components of 24 hour energy expenditure. There are several limitations in the use DLW which include (a) problems related to use of Food Quotients instead of Respiratory Quotients in the conversion of CO_2 production rates to energy expenditure, (b) problems associated with sequestration of the isotope during *de novo* synthesis of body tissue and (c) corrections that need to be made to provide for reliable estimates of fractionation of the isotope during transpiration or transcutaneous water losses in sweating. All of these may be important issues when the technique is used in developing countries to assess energy expenditure of free living subjects in tropical environments and in the presence of high levels physical activity. The obvious advantages of DLW method is the safe application of this technique to estimate energy requirements of pregnant and lactating mothers as well as young infants and children. In addition, the method provides for a measure of the body composition of the individual and in breast fed infants also provides estimates of breast milk production rates. In summary, the DLW method is an elegant, but safe method for measuring total energy expenditure of a wide variety of free living individuals in developing countries and has a number of advantages which have to be balanced against the numerous disadvantages, high on the list being the enormous costs of the isotopes and analytical systems. However, DLW can be used to obtain reliable estimates of total energy expenditure and body composition in limited numbers of adult men and women and can then be used to validate a wide range of simpler, cheaper techniques which may have a wider application in developing countries.

Other stable isotope studies

The stable isotopic tracer first used in biological or nutritional studies is ^{15}Nitrogen. Schonheimer, who is considered the father of stable isotopic techniques in biology initiated the use of ^{15}N as early as 1937. Waterlow extensively used ^{15}N labelled amino acids such as glycine to look at protein synthesis and breakdown and estimate protein turnover rates in well nourished and malnourished subjects (3). ^{15}N labels are being replaced by ^{13}Carbon labels even for protein turnover studies with ^{13}C leucine as a favourite tracer. ^{13}C compounds are becoming increasingly popular for isotopic tracer studies because they are

cheaper and far more versatile. ^{13}C labelled cereal (rice) has been used to study intestinal absorption and to estimate intestinal losses in malnourished children with diarrhoea. ^{13}C labelled triolien has been used to demonstrate that variations in the dietary intake of fat will result in the mammary gland defending milk production and fat secretion when faced with restricted supply of fat in the diet both by converting more carbohydrate to milk fat and by reducing the oxidation of dietary fat. ^{13}C compounds have also been used to study cholesterol metabolism in human subjects.

The most elegant experiments using stable isotopic tracers which are of considerable relevance to developing countries are those which have been used to prove the `essentiality' of amino acids in the diet. These exiting results from the CNRC Houston indicate that short term feeding of proteins uniformly labelled with $^{13}C$ followed by the analysis of a rapidly turning over plasma protein can be used as an *in vivo* probe of `conditional essential' for individual amino acids during periods of development and growth or in relation to changes in levels of dietary energy intake.

Stable isotopes are thus emerging as safe, silent tracers which are ideal tools for nutritional research in humans. The nature of the problems that these newly emerging tools can be used to extensively investigate are those of particular interest to developing countries. The use of these stable isotopic tracers is likely to throw light on nutritional problems of poorer countries if systematic efforts are made to design studies using these tracers to address issues which are a priority in third world countries.

Acknowledgement

Support provided by the Department of Science & Technology, Government of India to establish the Stable Isotope facility in the Nutrition Research Centre, Bangalore. The Isotope Ratio Mass Spectrometers were supplied and installed by Europa Scientific, Crew, UK.

References

1. FAO/WHO/UNU Energy and Protein Requirements. Tech. Rep. Ser. 724. WHO, Geneva, 1985.
2. Lifson N, McClintock R. Theory of use of turnover rates of body water for measuring energy and material balance. J Theor Biol, 1966; 12: 46-74.
3. Waterlow JC, *et al.* Protein turnover in mammalian tissues and in the whole body; North-Holland, Amsterdam, 1978.

Proc 6th ACN 1991: 117-119

Qualitative methods in nutrition research

Peter Heywood

Nutrition Programme, The University of Queensland, Australia

Introduction

Those who make decisions about plans and programmes to promote change in the nutrition situation require accurate, reliable and timely information. Whilst it may often not be ideal, there is usually at least some information from surveys and routinely collected data about **what** the disease problems are, **how many** people are affected and **where**. However, information about **why** the problem exists, particularly when the focus is on behaviour, is usually not available from these sources. This latter type of information is usually **qualitative** in nature and provides descriptions and ideas about why people do and do not behave in certain ways. It has implications for the design of new programmes and the modification of those already underway.

Nutrition has much to gain from the use of qualitative methods. However, the traditional basis of nutrition in biomedical science means that nutritionists are much more likely to have training in quantitative methods, particularly those found in epidemiology. At the same time they are unlikely to have training in qualitative approaches to gathering information. In addition, those with a biomedical science orientation, because of their narrow quantitative methods bias, often have concerns about the rigour of qualitative methods and the representativeness of the information obtained through their use.

In this paper the qualitative methods most appropriate for use in nutrition are briefly described and the concerns most frequently raised about their use are discussed.

Qualitative methods of gathering information

The basic activities involved in obtaining qualitative information are to observe what people do, talk to them and listen to what they say, and record and analyse the information obtained. Social scientists use these activities in three basic methods - observation, in-depth interviews of individuals, and focus group discussion (1,2,3).

Observation means just that, and begins the moment the observer enters any situation. Initially the observations will be very general. They will include information about the physical setting, who is there (including age and gender of those present), what they are doing, differences between people, and so on. What a particular observer sees will be influenced by their background on experience. Thus, it is important to develop a general model or list of questions that serve as a guide for observations, to record the observations made, organise the information, interpret it and then, using the next method to be described, to discuss the observations and their meaning with others.

Interviews with individuals are the central activity of qualitative methods. The general approach is highly derivative of that used by anthropologists and other social scientists with an interest in qualitative information. The content of interviews depends on the objectives

of the study and what information is already available. The interviews are carried out in considerable depth and the responses are open-ended. The interview may be completely unstructured or carried out using an interview guide derived from the conceptual framework (see below) for the investigation. The information is recorded and later analysed and interpreted.

Focus groups are discussions in a small group on a specific topic guided by a moderator. The role of the moderator is to guide the group discussions to increase focus and depth on a specific topic. Focus groups are most appropriate where the amount of material to be discussed is relatively limited and specific; group interaction is likely to stimulate a greater range of responses; cost and time mean that individual interviews are not possible, and the subject matter to be discussed is not so sensitive that respondents will be inhibited in their discussion. Focus group interviews are carried out using a topic or interview guide derived from the conceptual framework. Again, the information is recorded and later analysed and interpreted.

Conceptual frameworks

Conceptual frameworks are developed to summarise existing information about the phenomena of interest. The amount of detail in the initial framework will depend on the amount of information available initially. Where little information is available it may be very limited. In other cases where considerable information is available from other sources the initial framework may be quite elaborate. The most important role of the framework is as a source of hypotheses about the phenomena and it thus serves as a guide for the content of the observations and interviews. As new information is gathered it is analysed and evaluated against the framework. This evaluation may suggest that new information is needed and/or that the framework should be modified. This will also suggest new hypotheses and what additional information is needed in another round of interviews and observations. Thus, the process of developing a framework, obtaining information, modifying the framework and obtaining new information is a continuous and iterative one. The iterative nature of this process is a critical aspect of qualitative investigations.

Issues in the use of qualitative methods

The primary issues which concern the broader nutrition community about qualitative methods are the apparent lack of rigour and the representativeness of the information obtained.

Lack of rigour

Reservations about the lack of rigour vary with the disciplinary background. Most scientists are trained within the narrow methodological confines of a single discipline. Those from biomedicine and other quantitative fields have considerable reservations about qualitative methods because the approach is so diffferent. At the same time, social scientists also have reservations about the use of qualitative methods by groups such as nutritionists because, almost by definition, use of these methods by the uninitiated results in unreliable and invalid information.

The issue here is not that particular methods should be used naively. It is that all investigators have a responsibility to ensure that the information obtained in any investigation is of a quality suitable for the purpose for which it is intended. A vital approach to ensuring quality of data in qualitative methods is triangulation and this is discussed further below.

Representativeness of information

Because the gathering and analysis of qualitative information, particularly by interview, is very labour intensive and time consuming it is usually not possible to use large samples of the population. Investigators are also dependent on the compliance of the particular people selected for interview. In this situation it is most important to be aware of, and to avoid, bias. Bias can result from distortions in sampling and in the information actually collected. It can result from distortions in sampling situations, time periods and people. The most important issue is to be aware of the ways in which bias may enter any investigation and to devise strategies to minimise it.

Triangulation

Triangulation is the use of a number of different approaches to any particular phenomenon. It involves comparing and complementing information from different sources and can be achieved in a number of different dimensions. For example, it can be achieved by using different sources of data and information, different disciplinary and theoretical perspectives, different methods of obtaining information, different types of subjects, and subjects drawn from different locations. The ultimate aim of using triangulation is to increase confidence in the information obtained and the interpretations made. Thus, to the extent that information from different investigators, sources and approaches is congruent there is increased confidence that it represents the actual situation. To the extent that they are not congruent, confidence is decreased. It is a vital technique in the use of qualitative information as it provides a way to minimise the possibility that a study's findings are simply an artefact of a single method, a single data source or a single investigator's bias (4).

Conclusion

Qualitative methods represent a new method for most nutritionists. Nevertheless, they have much to offer those involved in the design and evaluation of programmes. There is a need to provide these skills to nutritionists working in both service and research to assist them to obtain reliable information about why people are behaving in certain ways so that more effective intervention programmes can be designed and implemented.

References

1. Jorgensen DL. Participant observation: a methodology for human studies. Newbury Park: Sage Publications. 1989.
2. Patton MQ. Qualitative evaluation methods. London: Sage Publications. 1980.
3. Debus M. Handbook for excellence in focus group research. Washington: Academy for Educational Development.
4. Denzin NK. Sociological methods. A sourcebook. London: Butterworths. 1987.

Proc 6th ACN 1991: 120-127

Severe protein-energy malnutrition in urban Dhaka and their response to treatment

Sultana Khanum and Md Mostafa

Children's Nutrition Unit, Save the Children Fund (UK), Dhaka, Bangladesh

Introduction

According to a recent nutrition survey in Bangladesh, 18% of the 6-60 months age group suffer from severe protein-energy malnutrition (PEM) (1). These data are broadly similar to those in other national nutrition surveys dating back to 1976, suggesting that the problem of PEM persists and is still one of the major causes of death in infants and young children (2, 3, 4). Patients with severe PEM, particularly those with complications, are medical emergencies and require immediate treatment in order to prevent death and initiate the recovery process. We have studied aspects of nutrition rehabilitation in the Children Nutrition Unit (CNU) situated in Dhaka, the capital city of Bangladesh. The estimated total population is around 5-6 million. CNU has a 60-bed acute admission ward for children with severe PEM defined as nutritional oedema or wt/age < 50% and wt/ht < than 60% of Harvard growth standard (5).

A previous study (6) with these children showed that 1 child in every 7 had no father, 1 in every 13 had no mother, 20% mothers worked as domestic aid, 52% fathers were either transport workers or day labourers, 27% fathers and 12% mothers were literate, a greater number of females was admitted, 55% were either the first or second born, bottle-feeding was common and practised by 42% of mothers. About 57% marasmic cases were bottle-fed, and most parents earned less than Taka 1500 (US $50) per month. This paper describes PEM cases and their response to treatment in an urban nutrition rehabilitation centre.

Patients and methods

Severe cases of PEM children, age between 0-60 months admitted at CNU over a period of 5 years (1984 - 1988) were studied. On admission, weight, height and mid-upper arm circumference (MUAC) were measured. The nutritional status of patients was assessed by wt/age (below 1 year) and wt/ht achievements with reference to the Harvard Standard (7), and the presence or absence of oedema above 1 year. All children with oedema and all those with or without oedema, who were only 60% wt/ht or less, were classified as severely malnourished and were admitted to the in-patient unit for intensive care and treatment which included nutritional rehabilitation.

Laboratory studies at the time of admission included total plasma protein, haematocrit, urinalysis and microscopic examination of the stool for blood, pus cells, ova and parasites. Throat swabs and samples of blood, stool and urine were routinely taken for bacteriologic cultures. Mantoux test, and a chest radiograph was performed in all cases. Pulmonary tuberculosis was tentatively diagnosed when susggestive radiograph was associated with a constant clinical pattern such as positive mantoux test, unexplained fever in the hospital or growth failure

despite an adequate energy intake and no clinical signs of malabsorption.

Recovery diets

The aim was to achieve an energy intake of 100-120 kcal/kg/day in the first week and there after, 150-200 kcal/kg/day with approximately 2.5g protein/kg/day. The diet consisted of dried skimmed milk reconstituted with oil and sugar (100 ml = 100 kcal) initially given day and night. During the first week the amount fed was 90-100 ml/kg/day, then increasing gradually to 120-200 ml/kg/day in 4-6 feeds a day. Solid, cooked meal was offered from the first week ; some children refused solids initiallly but within a few days their appetite returned and solid diets were taken up to four times daily ad lib.

Anorexic patients were fed by naso-gastric tubes initially. In addition to the diets, vitamin supplements, oral iron from week 2, potassium chloride and magnesium sulphate were given routinely. Severe or moderate dehydration was treated with either i/v half-strength normal saline or orally as appropriate. Hypoglycaemia (blood glucose < 40mg/dl) or hypothermia (rectal temp. < 96 F) if present, were treated with appropriate measures. Blood transfusion or packed cell was given if PCV was less than 20%. Dietary intakes were measured by weighing each plate of food and left over.

The body weight was measured and recorded at the same time each day, by the same person. All infections were identified and treated with appropriate antibiotics. Patients were discharged when they achieved 80% wt/ht. Mean duration of hospitalisation to reach this criterion was 21 ± 5 days. Mothers stayed with their babies and received regular instruction on nutrition and basic health care. A group of children (460) among these were followed up at home 2 years after discharge. Results are expressed in proportion, and mean ± SD. Chi square test was used for statistical significance test.

Results

The mean age of the patients was 17 ± 15 months for marasmus (M) and 29 ± 17 months for kwashiorkor (K) and marasmic-kwashiorkor (MK). According to Wellcome Classification, 380 (18%) were maramus, 443 (20%) were kwashiorkor and 1313 (62%) were marasmic-kwashiorkor. Their mean wt/age were 39 ± 5% for maramus, 52 ± 9% for kwashiorkor and 46± 9% for MK. The mean wt/ht was 62 ± 6% for M, 73 ± 8% for K and 66 ± 8% for MK. The mean ht/age was 80 ± 6% for M, 88 ± 4% for K and 80 ± 6% for MK. The mean mid-upper arm circumference for M was 9 ± 3 cm, for K and Mk 10 ± 5 cm as shown in Table 1. Their wt/age, wt/ht and ht/age were very low and

TABLE 1

Nutritional status of PEM children based on Wellcome classification on admission at CNU (Mean ± SD) compared with 50th Centile Harvard Standard

Age and nutrition Status	Marasmus (M) n = 380 (18%)	Marasmic Kwashiorkor (MK) n = 1313 (62%)	Kwashiorkor (K) n = 443 (30%)
Age in months	17 ± 15	29 ± 17	29 ± 17
Wt/Age (%)	39 ± 6	46 ± 9	52 ± 9
Wt/Ht (%)	62 ± 6	66 ± 8	73 ± 9
Ht/Age (%)	80 ± 6	80 ± 6	88 ± 4
MUAC in cm	9 ± 3	10 ± 5	10 ± 5

there were evidence of both stunting and wasting in these children.

Prevalence of infections as shown in Table 2 were: overall, 25% had diarrhoea with dehydration but there was significant difference between M vs MK or K ($p < 0.001$); 16% had tuberculosis, but the difference was significant, M vs MK and K; more marasmics had TB ($p < 0.001$). Significant difference were also observed between the 3 types of PEM in cases of *Giardia lamblia* ($p < 0.05$), *Ascaris lumbricoides*, *Trichuris trichuria* and *Anchylostoma duodenale*, M vs Mk and K ($p < 0.001$). The lower prevalence of worm infection in marasmics was probably because they were younger, 90% had 1 infection and 80% had 2 or more infections.

The mean plasma total protein was 6.0 ± 2.0 g/dl for M, 4.8 ± 1.0 g/dl for MK and 4.5 ± 1.0 g/dl in K. Mean haematocrit was 30 ± 5% in M, 25 ± 5 % in MK and 24 ± 1 in K. M vs MK or K for these values were signifcantly different ($p < 0.001$). 45% had enlarged liver, 15% with dermatosis, 33% hair depigmentation, 66% had xerophthalmia and 40% had angular stomatitis. In all these conditions (more prevalent in MK and K) there was significant difference between M vs MK or K ($p < 0.001$).

Table 3 indicates mean energy intake (kcal/kg/day) and weight gain (g/kg/day) in week 2 during treatment.

TABLE 2
Prevalence of infections on admission by types of PEM

Infections	M (n=380) %	MK (n=1312) %	K (n=443) %	All cases (N=2135) %
Diarrhoea with dehydration	35	24	15	25**
Tuberculosis	24	15	9	16 **
Bronchopneumonia	64	69	70	68
URTI	41	48	49	47
Urinary tract Infection	19	25	23	23*
Septicaemia	12	12	11	12
Entamoeba histolytica	36	37	40	37
Giardia lamblia	16	23	22	21*
Ascaris lumbricoides	26	44	45	41*
Trichuris trichuria	5	19	25	17**
Anchylostoma duodenale	6	21	18	16*
Otitis media	22	24	20	23
Skin Sores	12	13	15	13

* M VS MK or K, $p < 0.05$
** M VS MK or K, $p < 0.001$

Both energy intake (192 ± 38) and weight gain (11 ± 5) were more in marasmic cases than in MK (163 ± 33) (10 ± 4) and K (138 ± 25)(8 ± 4) that is, for M vs MK and K significant difference were observed in energy intake ($p < 0.05$) and weight gain ($p < 0.001$).

Overall mortality rate was 5.0% (107), 3.5% (70) left against medical advice and 91.7% (1958) were discharged. There were no significant difference in the mortality among types of PEM.

Table 4 shows mortality risk of

TABLE 3
Mean weight gain (WG) and energy intake (EI) by type of PEM (Mean ± SD)

	WEEK 2		
PEM	N	WG(g/kg/day)	EI(kcal/kg/day)
Marasmus (M)	214	11.1 ± 5.0	192 ± 38
Marasmic-Kwashiorkor(MK)	890	10.1 ± 4.5	163 ± 33
Kwashiorkor (K)	118	8.7 ± 4.0	138 ± 25

M vs MK and K: EI = $P < 0.05$ WG = $p < 0.001$

TABLE 4
Mortality risk of diarrhoea, dehydration, septicaemia, tuberculosis, pneumonia and severe anaemia

Conditions	Infection present			Infection absent		
	Died n	Alive n	% Died	Died n	Alive n	% Died
Diarrhoea with dehydration	83	448	(18.5)**	76	146	(5.2)**
Septicaemia	26	206	(12.6)**	144	1906	(7.6)**
Pneumonary tuberculosis	37	320	(11.5)*	118	1653	(7.1)*
Bronchopneumonia (Excluding TB)	120	1143	(10.4)**	50	809	(5.7)**
Severe anaemia	104	1063	(9.7)*	66	949	(6.9)*

* $p < 0.05$ ** $p < 0.001$

infections present on admission. Among the deaths, patients with diarrhoea and dehydration, septicaemia, miliary TB, bronchopneumonia (post-measles and others), and severe anaemia (before blood transfusion) were at greater mortality risk.

Patients with more than 2 infections, younger children (age below 18 months), very wasted children, wt/ht below 50% Harvard Median had greater mortality risk, and most deaths occurred within 72 hours of admission.

Anthropometric measurements on nutritional status of the follow-up group (n=220) (i.e. those who were found in the follow-up search two years after discharge) were compared with the values for OPD-matched controls (n=150) and sibling control group (n=130) aged between 12 and 60 months living under similar conditions. Nutritional status of those found alive was satisfactory. Their mean wt/ht was 90% and 88 percent of children were above 80% wt/ht (Table 5). Even the siblings of study group were in better nutritional status (mean wt/ht was 87%) compared to OPD control (mean wt/ht was 76%).

Discussion

The children admitted were chronically malnourished as well as wasted, ie, low weight-for-height and there was a distinct difference in the mean age on admission between children with marasmus and those with kwashiorkor and marasmic-kwashiorkor. This supports the view of different pathogenesis of marasmus and kwashiorkor (9-12). The high prevalence of infection is comparable with our previous finding (13) and findings from Lesotho (14) and well documented by various authors (15, 16). These findings justify our routine use of broad-spectrum antibiotics in severe PEM. The observed incidence of entamoeba histolytica (37%) and Giardiasis (21%) would support treatment with metronidazole and use of antihelmentics to treat worm treatment. Our mortality of 5% however appears to be very low in contrast to our previous report (21% died) (13) and reports from Lesotho (25%) and other hospitals in Sub-Saharan Africa viz. Zambia (24%) and Nigeria (28%) (14, 17, 18). In some local hospitals in Dhaka and in Kanti children's hospsital in Nepal, high mortality (25%-30%)

TABLE 5
Comparison of percent Harvard weight-for-height of those found alive with matched OPD control and siblings control groups (8)

Group	Percentage Harvard Standard Wt/Ht					
	< 69	70-79	80-89	90-99	100+	Mean Wt/Ht ± SD
Found alive n=220	0	11.5	38.4	36.5	13.6	90 ± 5.1*
OPD-matched control n=150	15	41.1	40.5	2.4	0	76 ± 7.2*
Sibling control n=150	0	10.5	57	23	9.5	87 ± 7.7*

* ($p < 0.05$)

among severe PEM has been reported (unpublished). The most life-threatening complications of severe PEM which we are reporting here as mortality risk (diarrhoea and dehydration, pneumonia, septicaemia, tuberculosis and severe anaemia) have been reported years ago. We have been able to identify and successfully treat these serious complications only when they are detected in time, and we have been able to reduce mortality from 21% in 1978 to below 5% in 1988.

In surviving children growth rate was 8-11 g/kg body weight/day. Marasmic and marasmic-kwashiorkor cases showing better rate of weight gain than kwashiorkor in week 2 when all infections were treated. Our findings are comparable with these in other studies (19). During this phase, simple dietary modifications devised to increase energy intake facilitated fairly rapid weight gain (20).

The long term progress of our surviving children was better and similar to some other recent reports (21, 22). It was encouraging to note that the siblings of traced children had better nutritional status than OPD control even though they came from a similar socio-economic background indicating importance of mother's education and awareness. However, our result is in contrast with some previous disappointing reports (23-26).

It appears that in PEM children much of the reported high mortality during rehabilitation is probably avoidable. Too much refeeding during the early phase of treatment or failure to diagnose infection (because usual response to infection may be impaired), may be fatal. Priority must be given to treating infections, correcting fluid and electrolyte balances (27) preferably orally to avoid overload of circulation and treating severe anaemia and other nutrient deficiencies, xerophthalmia in particular. Our study indicates that many children from urban poor families who suffered from severe PEM and other complications can be successfully treated in nutrition rehabilitation centre and they can recover satisfactorily in home environment after initial treatment.

Prevention of PEM

The majority of the children with PEM were below 3 years of age. Age group below 18 months hold a greater mortality risk. Preventive strategy in short, should include identification of the vulnerable group at an early stage ie, (a) pregnant mothers to improve birth weight through maternal nutrition during pregnancy and lactation, to promote and project breast-feeding; (b) accessible and available health care centres where (i) infectious diseases can be prevented and treated, (ii) nutrition rehabilitation centres, or other facilities where PEM can be treated and mothers can get instructions on adequate and appropriate feeding practices, growth monitoring and child health care in general to prevent childhood malnutrition.

References

1. Bangladesh Bureau of Statistics. Report of the child nutrition status module: Bangladesh household expenditure survey 1985 - 86. Dhaka: Bangladesh Bureau of Statistics, 1987: 15-24.

2. Briend A, Wojtyniak B, Rowland MGM. Arm circumference and other factors in children at high risk of death in rural Bangladesh. Lancet 1987; 2: 725-27.

3. Chen LC, Chowdhury AKAM, Huffman SL. Anthropometric assessment of energy-protein malnutrition and subsequent risk of mortality among preschool-aged children. Am J Clin Nutr 1980; 33: 1836-45.

4. Fauveau V, Briend A, Chakraborty J, and Sardar MA. The contribution of severe malnutrition to child mortality in rural Bangladesh: Implications for targeting nutritional interventions. Food Nutr Bull 1990; 12(3): 215-219.
5. Waterlow JC. Classification and definition of protein calorie malnutrition. In: Beaton GH, Bengoa JM, eds. Nutrition in preventive medicine. Geneva: World Health Organization 1976; 531-55.
6. Khanum S. Factors contributing to protein-energy malnutrition in urban Dhaka. Bangladesh J Child Health 1985; 9(2): 80-89.
7. Stuart HC, Stevenson SS. In: Nelson WE, ed. Textbook of paediatrics. Philadelphia: W.B. Saunders, 1959: 12.
8. Khanum S, Kabir I. Survival and growth of severe protein-energy malnutrition children 2 years after nutrition rehabilitation in an urban nutrition centre in Bangladesh: letter. J Trop Paediatr 1989; 35: 3-4.
9. Alleyne GAO, Hay RW, Picou DI, Stanfied JP, Whitehead RG. Protein-energy malnutrition London: Edward Arnold, 1977.
10. Behar M, Viteri FE. Disturbances of nutrition I: protein-energy malnutrition. In: Jelliffe DB, Stanfield JP, eds. Diseases of children in the subtropics and tropic. London: Edward Arnold, 1978: 196-221.
11. Ebrahim GJ. Paediatric practice in developing countries. London: Macmillan Press, 1981.
12. McLaren DS. Protein-energy malnutrition (PEM). In: McLaren DS, Burman D, eds. Textbook of paediatric nutrition. Edinburgh: Churchill Livingstone, 1982: 103-13.
13. Brown KH, Gilman RH, Gaffar A *et al.* Infections associated with severe protein-energy malnutrition in hospitalised infants and children. Nutr Res 1981; 1: 33-46.
14. Tolboom JJM, Ralitapole-Maruping AP, Kabir H, Molatseli P, Anderson J. Severe protein-energy malnutrition in lestho, death and survival in hospital, clinical findings. Trop Geog Med 1986; 38: 351-358.
15. Morehead CD, Morehead M, Allea DM, Olson RE. Bacterial infection in malnourished children. Environtl Child Health 1974; 141-147.
16. Scrimshaw NS, Taylor CE, Gordon JE. Interaction of nutrition and infection. Geneva: WHO, 1968.
17. Khan AA, Gupta BM. A study of malnourished children in children's hospital Lusaka (Zambia). J Trop pediatr Environtl Child Health 1979; 25: 42-5.
18. Laditan AAO, Tindimebwa G. The protein-energy malnourished child in a Nigerian teaching hospital. J Trop Pediatr 1983; 29: 61-4.
19. Ashworth A, Bell R, James WPT, Waterlow JC. Calorie requirements of children recovering from protein calorie malnutrition. Lancet 1968; 2: 600-603.
20. Ashworth A. Practical aspects of dietary management during rehabilitation from severe protein-energy malnutrition. J Hum Nutr 1980; 34: 360-369.
21. Van Roosmalen-Wiebenga MW, Kusin JA. Nutrition rehabilitation in hospital a waste of time and money ? Evaluation of nutrition rehabilitation in a rural district hospital in South West Tanzania II: long term results. J Trop Pediatr 1987; 33: 24-8.
22. Hennard P, Beghin Bissuyt M. Long term follow-up of severe protein-energy malnutrition in Eastern

Zaire. J Trop Pediatr 1987; 33: 10-12.

23. Beghin ID, Viteri FW. Nutrition rehabilitation centres: an evaluation of their performance. J Trop Pediatr 1973; 19: 215-19.
24. Beaudry-Darisme M, Lathan MC. Nutrition rehabilitation centres: An evaluation of their performance. J Trop Pediatr 1973; 19: 299-332.
25. Scrimshaw NS. Comments on nutrition rehabilitation centre programmes. In: Underwood BA, ed. Nutrition intervention strategies. London: Academic Press, 1983: 201-5.
26. Cutting WAM. Nutrition rehabililtation. In: McLaren DS, ed. Nutrition of the community. Chichester and New York: Wiley-Interscience, 1983: 321-37.
27. The treatment and management of severe protein-energy malnutrition. Geneva: World Health Organization, 1981.

Proc 6th ACN 1991: 128-129

The family as the unit in community nutritional surveys

AE Dugdale and Linda Alsop-Shields

Human Nutrition Research Group, Department of Child Health, University of Queensland, St Lucia Q 4067, Australia

Introduction

Nutritional surveys should not only find the prevalence of malnutrition but also ways to correct the problem. Conventional surveys select an 'at risk' group, such as school children or toddlers. They find the prevalence of malnutrition in this group, but seldom elucidate the cause. The family is the primary determinant of nutritional status, so we can study both the prevalence and causes of malnutrition by using families rather than individuals as the sampling unit (1). In this paper we show how child nutrition is determined by families and then give examples of patterns of nutrition within families.

Methods and results

We have data over a 40-year period from children at Cherbourg Aboriginal Community in Queensland, Australia and from this we can compare patterns of nutrition of children between families and within families over two generations (2). We have used data from the children and grandchildren in two families to demonstrate this. Many children in Family 1 were less than 90% W/A and the grandchildren showed the same pattern of malnutrition. Children and grandchildren in Family 2 were well nourished with no children under 90% W/A. The patterns of the nutrition of the children and grandchildren were similar but were very different from Family 1. Hospital admissions in the two families also showed major differences. Children and grandchildren in Family 1 had many admissions to hospital, the children and grandchildren in Family 2 had very few. These data show that the family has a large and continuing effect on growth and health of children. The growth of the children and grandchildren in Family 1 were poor and these children had many hospital admissions. The growth of children and grandchildren in Family 2 were good and they had few hospital admissions. We have done a separate study to find whether these differences are genetic or cultural (3). The pattern of growth and health is similar to the growth and health of the mother during her childhood, but has no resemblance to that of the father. This shows that cultural practices of the mother, rather than genetic influences, are the cause of this family effect.

We do not have data to demonstrate the way this information can be used in nutrition surveys and so shall consider three hypothetical families whose children have been found to be malnourished by a nutrition survey of a pre-school. In Family 1, the undernourished preschool child is one of six children, all of whom are malnourished, although the parents are well nourished. The most likely cause of the problem is dilution of maternal care with too many children and the solution is family planning. In Family 2, the index preschool child is malnourished

and so are the other two children and also the mother. There is no father to help support them. This family almost certainly has absolute poverty and this is the cause of the nutritional problem. In Family 3, the index preschool child is malnourished. There is only one other child who is well nourished and the parents are also well nourished. If social causes of deprivation can be excluded, then the most likely cause of the child's problem is chronic disease. In these three families, the detection of the undernourished preschool child did not help determine the cause of the problem, but the cause became obvious when the rest of the family was examined. Many other patterns of family nutrition are possible, and each could help diagnose the cause of nutritional problems.

Discussion

Surveys are still the best and often the only way of assessing health and nutrition of populations. The conventional method of studying an 'at risk' group is not the most efficient way of detecting nutritional problems and their causes. By using the family as the sampling unit we can detect both the problem and its cause. With family as the unit, much of the work will be done in the home, which may make for minor logistic difficulties, but the serendipitous information gained from a home visit will outweigh the extra effort. As the aim of surveys is to improve health and nutrition, family surveys may avoid the need for further studies before a plan of action is adopted.

References

1. Dugdale AE. Family anthropometry - a new method for determining community nutrition. Lancet 1985; 2:720.
2. Dugdale AE, Musgrave IA, Streatfield K. The changing growth of Aboriginal children. J Pediatr Child Health 1990; 26: 192-6.
3. Dugdale AE, Lovell S, Muller M. Growth during infancy of parents and their children. Ecol Food Nutr 1985; 14: 47-50.

Proc 6th ACN 1991: 130-132

Vitamin A nutritional status of children living in comparatively poor rural areas in China

Chang Ying and Cheng Lie

Department of Community Nutrition, the Institute of Nutrition and Food Hygiene, Chinese Academy of Preventive Medicine, Beijing 100050, People's Republic of China

Present vitamin A status of children in poor rural areas

It was reported (1) that in the early fifties, vitamin A deficiency was a serious problem, and was one of the major causes of blindness in children in China. But along with the development of national economy and medical care and health services extended to rural areas, e.g. the immunisation programme now covered 85% of children in every county of the country, and the programme includes BCG, Polio, DPT and measles vaccines. So the symptoms and signs of vitamin A deficiency were greatly reduced. In recent years there were very few cases of xerophthalmia seen even by the ophthalmologist. However the serum retinol level of rural preschool children reported by Chang Ying (2), Tian Qingchun (3) and Cheng (4) were quite low; the percentage of children whose serum retinol levels are less than 20 μg/dl were 37.1, 39.3 and 33.5% respectively.

Recent study on the nutritional status of 12,049 preschool children of comparatively poor rural areas in 18 study sites with an average income ranging from 200-500 yuan/capita/year (5), showed that the prevalence of conjunctival xerosis and corneal xerosis were 0.04% and 0.03% respectively. The prevalence of clinical vitamin A deficiency was 0.62%. The average vitamin A intake of 5211 two-five years old preschool children of the above-mentioned 18 study areas were 71.5, 59.0, 63.0 and 42.0% of the Chinese RDA.

Since vitamin A deficiency is usually associated with severe malnutrition, the body weight and height of the children were measured. The prevalence of wasting, stunting and low body weight as defined by the % of children whose weight-for-height, height-for-age and weight-for-age were lower than the 3rd percentile of the NCHS reference standard were as follows:

	males %	females %
wasting	2.7 - 8.0	3.3 - 8.3
stunting	21.4 - 78.0	18.8 - 78.1
low wt/age	11.6 - 49.1	12.5 - 48.3

The highest prevalence rate occurred in the 1-2 year age groups. So these children were in a state of chronic malnutrition instead of acute wasting type.

With such a background of vitamin A nutritional status of the rural preschool children, we are interested in knowing whether this condition will do any harm to the health of children including their body defence mechanism to infectious diseases. Thus a vitamin A supplementing trial was carried out.

Impact of vitamin A supplementation on childhood diarrhoea and respiratory diseases

One hundred and seventy-two 0.5-3.0 year old children in the mountainous area of Hebei province, where 33.6% of children under 3 years have serum retinol values less then 20 μg/dl and 8% less then 10 μg/dl, but without vitamin A deficiency eye symptoms and signs, were randomly assigned to either vitamin A supplementation group (n=98) or served as control (n=74) for one year. Capsules containing 200,000 IU vitamin A and 40 IU vitamin E and placebo containing ordinary vegetable oil were given to children of experimental and control group by the study supervisor at the beginning of the study and 6 months later. The occurrence and severity of diseases recalled by the mother over the previous 2 weeks were recorded by the trained local village doctors who visited the families every 2 weeks. The study supervisors checked the results every 2-3 months. The results showed that there were significant reductions in the incidence of diarrhea ($p<0.01$) and respiratory disease ($p<0.01$) in the children of experimental group compared to the control. Relative risk of diarrhea and respiratory disease was 2.6 and 3.6 times higher respectively in the control children. Serum retinol and IgA levels of experimental group were significantly higher than that of the control group ($p<0.01$) 8 weeks after first dose supplementation. A significant decrease in the percentage of children with low heights and weights was observed. It was concluded that the supplementation of large doses of vitamin A to the deficient children decreased the incidence and severity of diarrhoea and respiratory disease, and improved growth of those children, possibly through the enhancement of activity of the immune system. Now the same experiment is going on in some other places in order to obtain more information before the recommendation of the supplementation programme to the government.

Other intervention programmes implemented in the rural areas to improve the vitamin A nutritional status

1 Training of nutrition field workers: Any intervention programme needs man power to implement it. Since the local township and village doctors are lack of both nutrition knowledge and the experience of field work management, so during the last 5 years more than ten thousand field workers were trained by using the modified training package originated by FAO, called Nutrition and Food Field Work Management. Most of the trainees have participated in the nutrition project carried out in their hometown by using local resources.

2. Promotion of the home garden activities and domestic animal raising: In the rural areas, most of the foods are produced by the families themselves, so expending the soyabean cultivation and increasing the varieties of vegetables especially green leafy vegetables and fruits grown in home gardens and courtyards; these are promising ways to improve the quality of the family diet. In addition, by selling the surplus products produced in the garden, the income of the family can be increased, which in turn will increase the capability of the family to buy more varieties of foods. In many of our study sites these kinds of activities have progressed quite sucessfully and gradually spread to other parts of the country. However, the health impact of home gardening still needs to be identified.

3. Nutrition education: The improvement of nutritional status of the people relies on the awareness of people of their own nutrition problem and the intention to change their

behaviour, so nutrition education given to the public, especially to the mother is crucial for the improvement of the nutritional status of children. During the past years, although we have carried out some nutrition education activities, greater efforts are still required to fulfill the tremendous demand of the society.

References

1. Zhao Xi-He. Vitamin A status of Chinese Population. Proceedings of the Fifth Asian Congress of Nutrition, Osaka, Japan. Oct. 1987: 26-9.
2. Chang Ying. Unpublished Data.
3. Tian Qingchun *et al.* An assay on serum vitamin a level of 774 children in the countryside. Acta Nutrimenta Sinica 1988; 10(2): 192-4.
4. Cheng Lie *et al.* The impact of large doses of vitamin A supplementation on childhood diarrhoea and respiratory diseases. Acta Nutrimenta Sinica. (For Publishing).
5. Institute of Nutrition and Food Hygiene. Proceeding Report on Nutrition Surveillance and Improvement of Children in China (1985-1989).

Proc 6th ACN 1991: 133-136

Selenium, zinc, copper, taurine, magnesium and calcium concentrations in human breast milk and its relationship to infant growth

Ikuo Sato, Kenji Yamaguchi and Masayuki Totani

Division of Maternal and Child Health, The National Institute of Health and Nutrition, 1-23-1 Toyoma, Shinjuku-ku, Tokyo 162, Japan

Introduction

It is well-known that the pattern of nutrient constituents in human milk is the most suitable for the human infant because it meets the physiological requirements of the infant (1). Therefore, exact and complete knowledge of the composition of human milk is essential for understanding more precisely the nutrient requirements of the infant as well as for developing more adequately defined formulas to be used as a substitute for human milk. This study examined the concentrations of selenium, zinc, copper, magnesium, calcium and taurine in human milk, and their relationship to infant growth.

Materials and methods

Description of donors

The subjects were 304 healthy and well-nourished lactating women who lived in a local city (Nagano, Japan). The mothers delivered healthy full-term infants. They were of middle socioeconomic status and ranged in age from 22 to 35 years.

Collection of milk samples

The 304 mothers provided milk samples after feeding (hindmilk) in the morning. The samples were classified according to the stage of lactation. These seven stages were from 4 to 7, 8 to 30, 31 to 60, 61 to 90, 91 to 120, 121 to 150, and over 151 postnatal days.

Regarding the infants fed by mothers from 61 to 150 postnatal days (n=138), anthropometric indices were measured on the day of collection of milk samples. The growth of their infants were assessed by weight-for-age and height-for-age percentile of the Japanese reference. The infants were classified into 3 groups. Growth of the infants whose body weight or height was less than 25 percentile, from 25 to less than 75 percentile, and over 75 percentile were defined as `poor', `normal' and `well', respectively.

Analytical methods

The concentrations of Se were determined by fluorometric method, those of Zn and Cu by atomic absorption spectrophotometry after wet-ashing procedure, and those of taurine by amino acid analyzer.

Statistical methods

Pearson's correlation coefficients were calculated. Partial correlation coefficients among concentrations of each nutrient were calculated after adjustment for postnatal days. Differences between means were tested using

Student's t-test.

Results

Mean concentrations of selenium, zinc, copper and taurine in human milk decreased significantly at each stage of lactation, with the zinc and taurine concentrations showing greater decline. No change was observed in magnesium and calcium concentrations (Table 1). Significant decreases in the concentration of selenium, zinc, copper and taurine were observed at the first 3 stages of lactation (from 4 to 90 postnatal days).

To evaluate relationships that may exist among concentrations of nutrients in human milk, correlation coefficients were calculated. Partial correlation coefficients among concentrations of selenium, zinc, copper and taurine in human milk from 3 to 150 postnatal days adjusted for postnatal days were significant ($p<0.001$) except copper versus taurine concentrations (Table 2).

TABLE 1
Postnatal changes of nutrients in human milk

Stage of lactation (days)	Selenium ng/ml	Zinc µg/ml	Copper µg/ml
4 - 7	29 ± 7* (23)	5.5 ± 1.9 (22)	
8 - 30	21 ±4# (7)	3.1 ±0.4# (7)	0.37 ±0.11 (3)
31 - 60	18 ±4# (34)	1.5 ±0.8# (33)	0.27 ±0.05 (25)
61 - 90	15 ±4# (60)	1.2 ±0.5# (59)	0.22 ±0.05# (50)
91 -120	15 ±3 (109)	1.0 ±0.4# (111)	0.22 ±0.06 (78)
121-150	14 ±3 (48)	0.9 ±0.5 (49)	0.21 ±0.08 (38)
151-340	15 ±4 (21)	0.7 ±0.3 (23)	0.14 ±0.04 (19)

Stage of lactation (days)	Taurine µmoles/ml	Magnesium µg/ml	Calcium mg/ml
4 - 7	0.67 ±0.13 (24)	29 ±6 (22)	0.28 ±0.07 (22)
8 - 30	0.49 ±0.21# (5)	30 ±4 (4)	0.23 ±0.05 (4)
31 - 60	0.36 ±0.14# (33)	29 ±4 (8)	0.31 ±0.06 (8)
61 - 90	0.32 ±0.11 (42)	28 ±7 (13)	0.28 ±0.04 (13)
91 -120	0.30 ±0.09 (60)	28 ±5 (50)	0.29 ±0.04 (50)
121-150	0.27 ±0.11 (28)	31 ±4 (19)	0.30 ±0.04 (19)
151-340	0.28 ±0.15 (19)	34 ±4 (8)	0.29 ±0.06 (8)

* Mean±SD. Number of samples in parentheses

\# Significantly different from the previous stage of lactation ($p<0.05$)

TABLE 2
Correlations among nutrients in human milk adjusted for postnatal days (From 3 to 150 postnatal days)

Nutrients	Selenium	Zinc	Copper
Zn	0.466* (219)		
Cu	0.257* (178)	0.361* (181)	
Taurine	0.367* (199)	0.374* (200)	0.050 (159)

* $p<0.001$
Number of samples in parentheses

Table 3 shows mean and standard deviation of each nutrient in milk samples classified according to the growth of infants assessed on weight-for-age and height-for-age basis. This table also indicates frequency distributions of the infants in each category of growth. Zinc concentration in milk collected from mothers who had well-nourished infants on the basis of weight-for-age was significantly higher than the others.

Discussion

Although nutrient concentrations of the human milk obtained in this study were generally in agreement with previous reports in the literature (2-7) at all stages of lactation, a few authors (8, 9) reported different values. This discrepancy may be due to the methods of sample collection, and/or the sampling procedure. Another explanation of this discrepancy seen in these reports is considerable intraindividual

TABLE 3
Relationship between nutrient concentrations in human milk and infant growth

Nutrients	Weight			Height	
	poor[1] n=63	normal[2] n=58	well[3] n=17	poor n=64	normal n=56
Selenium (ng/ml)	15±4*	14±3	14±4	15±4	15±3
Zinc (μg/ml)	1.0±0.5[a]	1.0±0.5[b]	1.3±0.6[ab]	1.0±0.5	1.0±0.4
Copper (μg/ml)	0.21±0.07	0.20±0.05	0.20±0.06	0.21±0.07	0.20±0.05
Taurine (μmoles/ml)	0.27±0.10	0.29±0.09	0.27±0.01	0.27±0.10	0.29±0.09

*Mean±SD
Values within a row sharing a common superscript are significantly different ($p<0.05$)

[1] Less than 25 percentile of weight or height-for-age
[2] Over 25 and less than 75 percentile of weight or height-for-age
[3] Over 75 percentile of weight or height-for-age

variation of nutrient concentrations in human milk. Actually, in this study, intraindividual variation of nutrient concentrations was large, especially in the early stage of lactation.

Some authors reported that the intake of zinc and copper had no effect on their concentrations in human milk (5, 10). Others reported that zinc concentrations in human milk were influenced by maternal zinc intake within a physiological range (11). Whether the maternal nutrient intake influences the particular nutrient concentration in breast-milk or not is in dispute.

Zinc concentration of milk from the mothers of breast-fed infants with body weight over 75 percentile weight-for-age, was higher than that from the others. The improved growth of infants receiving zinc-supplemented formula has been reported (13). Intake of zinc in human milk may be related to growth of infant.

References

1. American Academy of Pediatrics. Breast-feeding, a commentary in celebration of the International Year of the Child, 1979. Pediatric 1978; 62: 591-601.
2. Hadjimarkos DM, Shearer TR. Selenium in mature human milk. Am J Clin Nutr 1973; 26: 583-5.
3. Butte NF, Garza C, Smith EO'B, Wills C, Nichols BL. Macro and trace-mineral intakes of exclusively breast-fed infants. Am J Clin Nutr 1987; 45: 42-8.
4. Salmenpera L, Perheentupa J, Pakarinen P, Siimes MA. Cu nutrition in infants during prolonged exclusive breast- feeding: low intake but rising serum concentrations of Cu and ceruloplasmin. Am J Clin Nutr 1986; 43: 251-7.
5. Moser PB, Reynolds RD. Dietary zinc intake and zinc concentrations of plasma, erythrocytes, and breast milk in antepartum and postpartum lactating and nonlactating women: a longitudinal study. Am J Clin Nutr 1983; 38: 101-8.
6. Picciano MF, Calkins EJ, Garrick JR, Deering RH. Milk and mineral intakes of breastfed infants. Acta Paediatr Scand 1981; 70: 189-94.
7. Zaima K, Nishihara K, Kobayashi N. Taurine concentration in cord blood, maternal serum and breast milk. Sulfur-containing Amino Acids 1978; 1: 241-50.
8. Feeley RM, Eitenmiller RR, Jones JB, Barnhart HB. Copper, iron, and zinc contents of human milk at early stages of lactation. Am J Clin Nutr 1983; 37: 443-8.
9. Garza C, Johnson CA, Smith EO'B, Nichols BL. Changes in the nutrient composition of human milk during gradual weaning. Am J Clin Nutr 1983; 37: 61-5.
10. Vouri E, Makinenen SM, Kara R, Kuitunen P. The effect of the dietary intakes of copper, iron, manganese and zinc on the trace element content of human milk. Am J Clin Nutr 1980; 33: 227-31.
11. Krebs NF, Hambidge KM, Jacobs MA, Rasbach, JO. The effect of a dietary zinc supplement during lactation on longitudinal changes in maternal zinc status and milk zinc concentrations. Am J Clin Nutr 1985; 41: 560-70.
12. Walravens PA, Hambidge KM. Growth of infants fed a zinc supplemented formula. Am J Clin Nutr 1976; 29: 1114-21.

Proc 6th ACN 1991: 137-140

Food habits modification for improvement of maternal and child nutrition in rural Thailand

Kraisid Tontisirin, Jintana Yhoung-Aree and Aree Valyasevi

Faculty of Medicine, Ramathibodi Hospital and the Institute of Nutrition, Mahidol University; Faculty of Medicine, Thammasat University, Bangkok, Thailand

Introduction

In the vast majority of developing nations, malnutrition persists among preschool children, pregnant and lactating women. These groups often reside in rural poor areas, possess inappropriate food habits, and lack nutritional awareness. Considering the pivotal importance of food habits in the malnutrition/infection cycle, Thailand implemented a food habits research and development effort from 1985-1989. The project was funded by the Australian Government, through the ASEAN Sub-Committee on Protein: Food Habits Research and Development. The Institute of Nutrition at Mahidol University (INMU) served as the project coordinator. This presentation gives an overview of the project's process, major results, and its transferable principles.

Purpose, objectives and study areas

The project's purpose was to improve the nutritional status of preschool children, pregnant and lactating women in Thailand's four major regions. The project's two main objectives were to identify food habit problems and their contributing factors among the target population, in addition to exploring appropriate behavioral modification approaches which could change undesirable food habits while strengthening desirable ones. The research area contained seven study sites as based on cultural, geographic and religious differences. The project called upon experts from five universities, one teachers' training college, and a provincial hospital. Their major roles were selecting study sites and the target population, and serving as research teams who worked with villagers to develop appropriate community-based intervention strategies. Each study site team covered 2 to 8 villages and 72 and 228 target households.

Design and methodology

The project used a systematic triple-A approach entailing **A**ssessment, **A**nalysis and **A**ction. Its phases, activities and results are as follows.

Phase 1: Assessment and analysis phase

Field researchers lived in the study villages for 4 to 8 months to gain an in-depth understanding of the target populations and their livelihoods; food habits and beliefs; food obtainment, selection and processing practices; as well as maternal and child nutritional behaviors. Research methods included participant observation with in-depth and informal interviewing, conversa-

tions and structured observations. Key informants comprised community leaders, local authorities and members of the target families. Such qualitative data were collected using structured open-ended guidelines and analyzed daily. Quantitative data were obtained concerning general community and target population characteristics using a standard structured questionnaire and record forms. Variables included such areas as standard demographic information, village health and social development profiles, economic levels, food availability, nutritional status and dietary intake.

Results pinpointed several food and related practices affecting general nutrition among the target population. These included inappropriate traditional beliefs about food, pregnancy and child development; food taboos/restrictions during pregnancy, lactation and child illness; incorrect or inadequate nutritional awareness; and the role of external forces (e.g., the elderly, mass media advertisements) on food selection and consumption. Over 90% of mothers, though, practised breast-feeding. Well-educated mothers correctly prepared and fed supplementary foods as suggested by health workers.

Phase 2: Solution (action) phase

Based on these findings, a four-fold model strategy was launched entailing Participatory Action Research (PAR), nutrition education, supportive activities and evaluation. In the first case, since community participation is fundamental for solving many local problems, **Participatory Action Research** (PAR) served as the project's operational approach. It covered five interactive steps where community members and researchers worked together as **project collaborators**. The first involved community selection and rapport building wherein researchers became accepted and concerned participants in each village. Second, researchers acted as stimulators to help villagers learn about their community's nutritional situation and its determinants. Step three involved working with villagers to determine appropriate programmes for solving community-identified problems. In step four, villagers and researchers prioritised potential intervention programmes based on existing needs and resources. The final step involved planning and undertaking the selected programmes using realistically attainable objectives.

Nutrition education rested on the developing and disseminating a total of approximately 14 separate print and interpersonal communication programmes. Media production utilised a people's participation approach to nutrition communication where villagers took an active part in producing those media which would be socioculturally appropriate and maximally accessible to target group members. Collectively, the media promoted new food habits and educated target group members through a process of creating new knowlegde; initiating new attitudes, perceptions and beliefs; and ending with the introduction of new or modified food and nutrition practices. For pregnant mothers, messages included information on foods required during pregnancy, the need for attending ante-natal clinics, and immunisations. Lactating mothers were encouraged to recognise and consume appropriate foods, especially animal protein and green leafy vegetables. For preschool children, messages aimed at caretakers and addressed such topics as colostrum, breast-feeding, supplementary food, nutritious snacks and foods to be consumed during illness.

Supportive activities were used as important mechanisms for increasing community participation and as a coordinating focus for existing government

health and nutrition programmes. The project's activities included developing new recipes or adapting existing ones; food production and preservation demonstrations; school lunch programme improvements; literacy campaigns; environmental sanitation campaigns; and basic health services.

The **evaluation** stage addressed both process and impact with activities being assessed before, during and after programme implementation for each study site. The common key indicators were scores on knowledge, attitude and practice (KAP) in nutrition and related aspects so as to evaluate media effectiveness and that of the model itself. A qualitative evaluation was also conducted to help explain quantitative data and assess people's participation in the project. Regarding impact, the project anticipated an improvement in the populations' nutritional status, especially among preschool children. Nutritional status was assessed by anthropometry, prevalence of deficiency signs, as well as 24-hour dietary recall.

Results

Similar trends in KAP improvement were observed in all study areas (as opposed to control areas). After one year of the solution trial, statistically significant to highly significant improvements were made in knowledge and attitudes towards proper food habits, food preservation, the dangers of eating potentially harmful foods, and the causes of malnutrition. Positive changes in some practices were also noted, such as eating a wide variety of foods during pregnancy and lactation, high quality food consumption during the postpartum period as well as during child illness, giving colostrum to newborn infants, supplementary feeding of infants, and food preservation. The nutritional status of preschool children also improved along with declining rates of nutritional deficiency symptoms and signs (e.g., angular stomatitis, night blindness). Other practices (e.g., consuming a low fat diet, early infant feeding, eating non-nutritious candies and snacks), however, showed little change due to deeply rooted and complex causal processes.

Nonetheless and aside from the nutrition intervention programme, health services also influenced food habits. In short, the better the service each mother received, the more likely she was to avoid undesirable food habits. After project implementation, results showed an increase in the number of mothers receiving ante-natal care at local health centres, where they received vaccinations, iron and vitamin supplementation and nutrition education.

Conclusion

To modify inappropriate food habits requires a model containing both biomedical as well as social science perspectives and methods. It also demands an accurate, early analysis of each community's socio-cultural, economic, political and physical environments. Projects also require a positive interactive atmosphere where responsibilities are shared by communities, local development organisers and project teams as **project collaborators**. The project also needs an evaluation approach which addresses both process and outcome measures. Nutritional messages and concrete supportive activities must match with village life and its members' interests. This is important because, ultimately, the community members are the one's who make the real difference. They are the ones who must change themselves.

References

1. Merican Z. ASEAN Food Habits: Final Report of the ASEAN Food

Habits Project. Kuala Lumpur: ASEAN Sub-Committee on Protein: Food Habits Research and Development, 1989.

2. Valyasevi A, Tontisirin K, Yhoung-Aree J and Dhanamitta S. Development for food habits modification in rural Thai. In: Proceedings of the Seventh ASEAN Workshop on Food Habits: Food Habits Research and Nutrition Improvement in ASEAN. Kuala Lumpur: ASEAN Sub-Committee on Protein: Food Habits Research and Development, 1990: 158-71.

Proc 6th ACN 1991: 141-147

Aging and nutrition: An overview with notes on their investigation and communication in developing countries

Noel W Solomons

Centre for Studies of Sensory Impairment, Aging and Metabolism (CeSSIAM), research branch for the National Committee for the Blind and Deaf of Guatemala, Guatemala City, Guatemala

Introduction

A variety of specific experience in gerontological nutrition from a diverse set of nations will be presented in this Symposium. The purpose of this paper is to present an overview from the developing countries of the world. Although Asia is a vast region which includes the barren expanses of Siberia, and the bustling industralized dynamos of Japan, Korea, Taiwan and Hong Kong, the majority of its population lives in the transitional nations of Thailand, Singapore, Malaysia, and China, or the less developed countries of the Indian Subcontinent, the IndoChinese Penninsula, and the archipelagos of the Philippines and Indonesia. The majority of the research experience of this author has been in Latin America. It is hoped that the general lessons and the points of view from the western hemisphere have relevance for the eastern hemisphere, as well. This paper presents a general overview of the problems and potentials in conducting research into the combined issues of aging and nutrition, with special notes on the opportunities and difficulties presented in transitional and developing nations of the Third World.

Demographics

Demographics are the most important factors directing health-related and human biological research in developing countries. Since World War II, the poor nations of the belt between the Tropic of Cancer and Tropic of Capricorn (and the poor sub-segments of temperate countries, as well, have experienced explosive population expansion (1, 2). This led to a population age-pyramid with a broad base with over half of the population being below 15 y. The associated high childhood mortality resulted in a significant reduction in the individuals that reached adulthood and were eligible for passage to the third and fourth ages of life. It is logical that a concern for child health and maternal well-being, especially that for the pregnant and lactating woman, has been predominant.

Through the last 50 years, the major concern has been maternal-child health (MCH), and the primary medical professionals have been pediatricians. Gerontology and geriatrics remained virtually unknown in the Third World. Recently, however, both the age-pyramids and public health concerns have begun to shift. A study by George C. Myers and Daniel O. Clark, of the Centre for Demographic Studies of Duke University, entitled "Geographic Distribution of Older Persons within Countries: An International Trend" (3), presented at the XIV International Congress of Gerontology in Acapulco, Mexico, looked at the

Latin America in the 1980s. In 1985, 11.8% of the Israeli population, 10.34% of the Japanese population, and 8.3% of the Cuban population were over 65 y. In India, the figure was 6.3%, whereas it was 4.3% in the Republic of Korea, and 5.7% in Chile.

Scientific development in developing countries

National underdevelopment is a global, if uneven, phenomenon that affects economic, financial, social, cultural, and educational spheres. Universities are the traditional repositories of both knowledge and investigation in a country. Given the multitudinous problems and limited resources, university research in developing countries has been eminently applied, in an effort to solve perceived problems. This has oriented the majority of investigators to the MCH domain. The other two models for health-related research in Third World, regional centers financed by the United Nations dependence and private investigative units, are present to a lesser degree.

Biomedical scientific development in scientifically-underdeveloped countries should seek three goals: (i) formation and training of young scientists; (ii) the creation of investigation of excellent quality; and (iii) communication of the research findings to the scientific and public health communities, both in the country of origin and to the world at-large. The Centre for Studies of Sensory Impairment, Aging and Metabolism (CeSSIAM), is a private research unit in Guatemala, founded in July 1985 in affiliation with the Committee for the Blind and Deaf of Guatemala. It was fortunate for the development of gerontological research that the term "aging" was included in the name (4). Acceptance of aging research was related to the fact that much of the concern for an eye hospital are ocular diseases of aging (such as glaucoma, cataract, retinopathies, maculopathies), and that the elderly are a group that may require institutional advocacy.

Not only in Guatemala, however, are biomedical scientists directing their attention to gerontology. This is occurring in other countries of the Latin American region with the argument being diverse: one concern is the density of the ignorance that currently exists about tropical gerontology. A second is a long-range concern for the utilisation of health services when the aging population has grown to larger proportions. A third is an interest in contributing, through collaborative research, to the understanding of human aging, per se. It is very common, moreover, that the themes addressed in Third World aging research relate to aspects of diet and nutrition (5). Malnutrition and nutritional deficiency states have long been recognised as problems in the developing world. This is one of the areas in which local expertise and international investigation have been developed. Thus, in the topic under consideration, the relative strengths in nutrition and dietetics are married to a chronic weakness in research in universities, regional centres and private research units of Third World countries, namely, that of aging biology investigation (6).

Research on the topic carries collateral benefits. It introduces new concepts into the minds of the investigators. New investigative tools and resources must be acquired. New scientific associations and communications are born. The introduction of gerontology into scientific circles in less developed countries is a contribution to scientific development, as the new horizons and intellectual stimulation injected should more than compensate for any distraction from the issues of maternal and child health.

What needs to be studied in aging biology and geriatric epidemiology in relation to diet and nutrition in developing counties?

It would be arrogant and presumptuous to generalise from a narrow experience in Central America and a brief history of personal involvement to the entire scope of needs in aging biology and geriatric epidemiology in relation to diet and nutrition in developing countries all around the globe. What is shown in Table 1 is a roster of descriptive topics. One must understand, in each region, the current situation as the first step in the process of developing aging and nutrition research. The areas of interest are: dietary habits, both current (in old age) and past (in younger adult life); the amount of internal migration, especially rural-to-urban; and current nutritional status both with respect to macro-and micronutrients.

TABLE 2

Paradigms of interactions between aging and nutrition

- Health status and functional capacity in relation to nutritional staus and dietary intake.
- Nutritional status and dietary intake in relation to health status and functional capacity.

Problems and methods in aging biology research

The goal of aging biology is to describe the processes that occur with time in the life of an organism (6). This can apply to everything from the most primitive multi-cellular organism to laboratory animal models to homosapiens. These present comments are restricted to human aging.

TABLE 1

Subjects for descriptive studies in the elderly

- The dietary habits of the elderly
- The life-long dietary patterns and changes during life
- The migration history in relationship to dietary changes
- The nutritional status in terms of body composition
- The nutritional status in terms of micronutrients

The topic under consideration implies the interaction of aging and nutrition. As shown in Table 2, this has two paradigms which look at the two directions of causal relations. The former looks at nutritional status and dietary intake as dependent variables and the latter considers these as the independent variables. The key to aging research is to identify the controlling, confounding and modifying variables, and use them to enhance the interpretation and conclusions.

The concepts of the nature of aging are various, and unresolved. Some theories see it as a developmental process, i.e. programmed cellular evolution and change (7). Others associate it with a deterioration process, i.e. exhausting of vitality through repetitive cell division and repair or environmental stress. Yet another school of thought subscribes to the theory that cumulative effect of disease of a lifetime is the cause of aging effect (8). If it were not for disease, according to this

theory, one would never age. With this scenario, the interaction of host, agent, and environment would become not only a determinant of disease, but also of aging.

Epidemiological evidence confirms that old age increases susceptibility to certain diseases (9). Genetics modulate the penetration of these conditions within a given age-group, but clearly cardiovascular and cerebrovascular diseases are more common in the older, as are most malignant tumours and most musculoskeletal diseases. More descriptive research in Third World geriatric epidemiology is warranted.

A number of important terms set the bases for thinking about aging and about aged populations. Since some confusion exists, it is useful to define these terms. **Life-span** is the maximum number of years that any member of the human species can possibly live; 120 y is considered to be the upper limit. **Life-expectancy** is the median survival of a given birth-cohort; that is, it is the age when only half of the individuals born in the same year will still be surviving and the other half will be deceased. Mortality from childhood infectious disease is a major determinant of death in the early years; childbirth-related death for women, and war casualty for men, can be the lethal hazards of the early adult years. When one is studying an aged population, one only has the survivors among the original birth cohort to be enrolled. **Selective mortality** is the consequence of the fact that persons with different exposures or different genetic constitutions are more likely to have died. One will never know how time would have affected the biology of individuals who did not survive for study (1). **Secular trends** are changes that are experienced by successive decade-groups or generations. Usually environmental or technological factors, i.e. the discovery of antibiotics, the change in food availability, the emergence of retroviral infection, etc., modulate secular trends over time (1).

The nature of different life-expectancies, of selective mortality, and of secular trends pose hazards for the conduct and interpretation of research into human aging biology. One mode of study are the **retrospective, life-history** studies. In this motif, a group of elderly of a given age(s) is enrolled and their present status (health, nutrition, dietary intake) is assessed and data on these same variables or on various exposures in early life are investigated. One pitfall is the reliability of data from self-reported histories. The use of archival data such as medical and dental records is more secure. However, it is to be borne in mind that the survivors represent less than half of those who were born together.

Another popular study design is the **cross-sectional or transverse** study of different age-groups. Here, a standardised and common examination and questionnaire protocol is applied to persons in decade-groups, i.e. 40-49 y, 50-59 y, 60-69 y, etc. One must bear in mind here that the cumulative (and selective) mortality is different in each progressively older group, and secular trends that affected the earlier or the latter groups are not — by definition — uniform over time.

The interpretation of retrospective studies and of cross-sectional studies with regard to universal and generalisable principles of human aging, is fraught with pitfalls. The difference between the average blood pressure in a group of 30 year-olds and in a group of 60 year-olds cannot be attributed, necessarily, to aging alone. On the other hand, some stressor may be present in the present group of the fourth decade, such that is does not represent what their elders had experienced. On the other hand, those with the higher blood pressures at age 30 might have had higher mortality during

30 years, distorting what might have been the process of age alone in the older group.

An obvious solution to these dilemmas would be to use a **longitudinal, prospective** aging study. In this model, a cohort would be enrolled in early life and followed until all had died. In this way, control for differential mortality and monitoring of secular-trend-producing events could be incorporated into the final interpretations with respect to the aging process, per se. In theory, this is the ideal approach. In practice, it is virtually impossible and impractical. The researchers will age and die, with — or in advance of — the subjects, and it would take 50 to 60 years to obtain the final conclusions.

A major error committed by persons who newly move into the field of aging research, let us say from pediatric research, is to ignore the pitfalls and caveats inherent in the various models of research design. Satisfactory conclusions can be derived, but only if the limitations are recognised.

Specific pitfalls and caveats for aging research in the developing world

The preceding section touched on the generic issues of conceptual definitions and methodological considerations in human aging biology. The countries of the Third World present some additional challenges for aging research, which are unique to the nature of poverty and underdevelopment.

Major issues are migration and secular trends. During the life-history of any individual, certain amount of instability in environmental exposure might have occurred. All persons who are 60 years of age today were born in 1931, a few years before the discovery of the sulfa drugs and a decade before the discovery of penicillin. However, in more highly contaminated and infectious disease-prone countries, the antibiotic age could have meant more in terms of allowing children to survive severe respiratory infections. The development of immunisations against childhood disease is another medical advance. Thus, for generations of persons born since 1950, a secular trend in reduced early mortality makes them less comparable to the prior generations.

Another unresolved issue is **chronological equivalency** across nations. If the aging process is, in part, a response to environmental factors, persons and populations would age at different rates in different climes. Even if intrinsic, genetic clockwork is the universal determinant of aging, different hereditary patterns, segregated by geography, could also produce differential gradients in aging. Thus, the methodological question comes up: What is the "equivalently aged" person in rural Laos as compared to a 70-year-old urban resident of Seoul?

The final problem both for "matching" populations and for making inferences about aging biology, in developing countries, is the more intensive operations of **selective survivorship** during the life-span of the surviving elderly of developing countries, given the mortal infectious diseases and nutritional deficiency states that undoubtedly thinned the population of their birth-cohort.

Potentials and pitfalls of cross-national and cross-cultural studies

The process of senescence and the propensity to physical deterioration and pathological conditions are poorly understood, as the foregoing discussion illustrates. We have mentioned a number of strategies for population enrollment for assessing aging biology, and each had a serious drawback. **Comparative research** is felt to be an

increasingly powerful tool in deciphering the enigmas of aging, specially, what is environmental, what is innate, and what is an interaction (10).

Cross-national and cross-cultural research in aging tries to isolate two dependent variables — the "intrinsic" aging process and pathological conditions of "old age" — in the context of different environments, different diets, and different nutriture histories. What is the influence on gut absorption at age 60 years of life-long intestinal helminthiases, of recurrent gastroenterities, and of chronic tropical enteropathy? What is the prevalence in menopausal women of hip fractures and vertebral compressions of a high calcium intake/active life-style society versus that of a low calcium/sedentary life-style population? These are the types of contrasts that are developed in cross-cultural and cross-national research.

Major multi-national initiatives in aging research have developed in recent years. Prof. Gary Andrews, of Flinders University in Australia, conducted a transnational study among the elderly in Fiji, Korea, Malaysia, and the Philippines (11). This with no major nutritional content. The Special Project for Research on Aging of the World Health Organization, based at the National Institute on Aging in Bethesda, Maryland, USA, has two components that relate to diet and nutrition: (i) determinants of successful aging; and (ii) hip fractures and osteoporosis.

Explicitly nutritional has been the project of the Concerted Action Project in Nutrition of the European Community - (EURONUT) entitled: "Nutrition of the Elderly" of the EEC. It compared nutrition and health among persons 75 years of age in European countries. A similar study, but to involve Malaysia, Thailand, Philippines, and Indonesia in Asia and Mexico, Brazil, and Guatemala in Latin America is being proposed by SEAMEO in conjunction with the EEC. Finally, a study that bridges industrialized and developing countries alike — at all latitudes and in all hemispheres — is the study "Dietary Habits of the Aged - A multicentre study", sponsored by the Committee II/8 of the International Union of Nutritional Sciences under the direction of Prof. Mark Wahlqvist, of Melbourne, Australia.

The mechanism of comparative research in aging is emerging as a powerful tool to develop insights on the interaction of environmental, life-style, the aging process and diseases of the aged. Ethical issues, however, must be addressed in relation to the potential for a severe asymmetry of public health benefits for some of the participant societies as compared to the others. This occurs when one country's experience with a condition of a low prevalence is contrasted with a condition of high prevalence in another. Instrinsically, the insights will be of much more importance for the health of the latter country or population! Moreover, the differential effort in finding and studying the cases (affected individuals) will be a consideration. Let us propose the case of two countries having populations of 10 million, but one with 15% of the population over 60 years of age (i.e. 150,000 elderly) and the other with 5% of its inhabitants in this age-group (i.e. 50,000). The rate of some condition of interest is 1 per 100 in the former nation, and 1 in 1000 in the latter nation among the elderly. It becomes obvious that there are 1500 potential subjects for study in the first region and only 50 in the second. Suppose, furthermore, that the former country is largely urban and the other primarily agrarian. Finding and enrolling subjects will be different. When it comes to disease such as hypertension, osteoporosis, Alzheimer's dementia, etc., the countries in the model with the large, concentrated elderly popula-

tion with high prevalence represent the industrialized nations whereas those with small, dispersed elderly with low rates are comprised of developing countries. In fairness to the investigators and the older citizens of the two regions, the asymmetries and inequalities in benefits and efforts must be taken into consideration in planning multi-national aging research.

Conclusion

There is realisation that the growing numbers of elderly in developing countries is justification for the study of gerontology. The interaction of aging and nutrition is a most relevant concern within the area of aging biology.

References

1. World Health Organization. Health of the Elderly Technical Report Series 779. Geneva, WHO, 1989.
2. Kinsella KG. Aging in the Third World. CIR Staff paper No 35, Washington D.C., Centre for International Research, U.S. Bureau of the Census, 1988.
3. Myers CG, Clarke DO. Geographic distribution of older persons with countries: An International Trend, Mimeo, Centre for Demographic Studies of Duke University, XIV International Congress of Gerontology in Acapulco, Mexico 1989.
4. Solomons NW. Siu ML, Mazariegos M. Gerontological research expanding in Guatemala. Ageing International 1987; 14:17-21.
5. ACC/SCN Symposium: Nutrition and Urbanization. Food and Nutrition Bulletin 1987 (part 1); 9:1-61; 1988 (part 2); 10:1-42.
6. Evered D, Whelan J (eds). Research and the Ageing Population, Ciba Foundation Symposium 134. Chichester: John Wiley & Sons, 1988.
7. Kirkwood TBL: Comparative and evolutionary aspects of longevity In: Finch CE, Schneider EL (eds) Handbook of the biology of aging, 2nd edition. New York: Van Nostand Reinhold, 1985, pp 27-44.
8. Grimsley-Evans J: Ageing and disease In: Evered D, Whelan J (eds) Research and the Ageing Population. Chichester: John Wiley & Sons, 1988, pp 38-47.
9. Body J, Brock DB, Williams TF. Trends in the health of the elderly population. Annual Reviews of Public Health 1987.
10. Kouris A, Wahlqvist ML, Davies L, Scrimshaw NW. Development of a survey instrument for the assessment of food habits and health in later life In: Mayal MF (ed), Dietetics in the 90s Role of dietitian/Nutritionist. John Libbey Eurotext Ltd 1988, pp 235-239.
11. Andrews G In: Evered D. Whelan J (eds) Research and the Ageing Population. Chichester: John Wiley & Sons, 1988, pp 38-47.

Proc 6th ACN 1991: 148-150

Nutrition and some chronic diseases in the elderly of China

Chen Xiao-shu

Institute of Nutrition and Food Hygiene, Chinese Academy of Preventive Medicine, 29 Nan Wei Road, Beijing, 100050 China

Introduction

During the past forty years, the average life expectancy in China increased from 35 to 70 years. The total amount of people over 60 years has reached about 85 million accounting for 8.2% of the total population. By the end of this twentieth century, their numbers will reach 130 million accounting for 11.0% of the total population.

Some chronic diseases such as cerebrovascular disease, cardiovascular disease and cancer have become the leading causes of death in many cities.

The authorities have paid more attention to geriatrics in the past decade, but the work which have been done on the nutrition for the elderly is too little to match the increasing demands. However, some investigations have been conducted on the aged people, e.g. comparing and analysing the diet patterns and living conditions of the persons enjoying longevity; investigating the trace elements levels in their environment and body tissues; studying the nutritional metabolic changes of the elderly people sufferring from some chronic diseases; studying the peroxidation status in the elderly, conducting dietary therapy and developing healthy foods etc. Liu Bian-sheng reported that the trace element spectrum is special in the environment of longevity areas. The distribution of longevity areas seems endemic. The diet of longevity people are mainly from plant origin with low fat, low calorie and low table salt. The distinguishing feature of longevity persons is always their involvement in physical labour and the attitude of enjoying their lives to the fullest.

The Chinese Nutrition Society has specifically proposed a Recommended Dietary Allowance for the middle-aged and elderly population.

The Department of Nutrition for the Elderly of the Institute of Nutrition and Food Hygiene has conducted a comprehensive nutrition survey in six regions with different dietary patterns involving about 2,000 people aged 45-75 years among urban and rural residents, herdsmen and fishermen in 1989-1990. The survey consisted of dietary survey, physical examination and blood and urine sample analysis. The items included in this survey are (i) medical history; (ii) dietary survey; (iii) clinical examination, blood pressure measurement, electrocardiogram, calcaneum roentgenogram and (iv) biochemical analysis for serum total cholesterol (TC), high density lipoprotein cholesterol (HDL-C), triglyceride (TG), serum and urine calcium etc.

The results showed that the components of the diet in different population groups are influenced by dietary habit and food supplies. Meat is the major component of animal food consumed by Beijing residents. Fish consumption

is the highest in fishing areas, averaging about 98 g and 47 g per day for Baoshan county (countryside of Shanghai) and Rongcheng county (Shandong province) respectively, but there is no milk and milk products in the diet of residents in the fishing areas. The consumption of meat and milk is highest but soybean consumption is almost zero in the residents of pastoral areas.

The energy intake of most of population are close to or approaching the Chinese RDA. The average protein intake of men was close to or beyond 90% of RDA, but the protein intake of 70% of the aged women did not reach 80% of RDA. The high quality protein (from animal and soybean) was available to about 48% of residents of fishing villages and pastoral areas, while only 12.1% was available to farmers.

The fat intake as a percentage of the total energy was over 30% in the city dwellers, but only 17% amongst farmers. In the herdsmen, the animal fat as a percentage of the total fat intake reached 80%, with little carotene and vitamin C intakes because of shortage of vegetables. The calcium intake of 50% of aged women even did not reach 400 mg per day.

Morbidity due to hypertension and coronary heart disease was the highest in the herdsmen and the lowest in the fishermen. Blood pressure was positively related to BMI, skinfold thickness and serum triglyceride. The prevalence of hypertension was higher among people whose daily salt intake was over 11 g ($p<0.050$). The prevalence of cardiovascular disease is positively related to age, the ratio of animal fat to total fat and BMI, and is negatively related to serum high density lipoprotein cholesterol by multi-regression statistics.

The risk of osteoporosis is higher in female than male with increasing age. About 50% of females older than 60 years old, were diagnosed as having osteoporosis. The relation of obesity and bone density showed that the higher the BMI the higher the bone density, and the bone fracture rate is lower among the obese. The prevalence of osteoporosis is related significantly to animal food intake. The bone density of the farmer is the lowest among the 5 regions.

In 1989, the findings of a study in cooperation with Cornell University and Institute of Nutrition and Food Hygiene on the examination of bone density of middle-aged and aged population in five areas with different calcium intakes showed that the bone density of the old women in the pastoral area of Inner Mongolia Autonomous Region was the highest owing to their higher calcium intakes.

These illustrate that there is a close interrelation of dietary pattern and nutritional status with the chronic diseases of the elderly.

In the later half of this century, the food consumption has increased consistently with the increasing food production in our country. Especially in big cities, animal food consumption increased very fast, such as in Beijing where the animal food consumption almost doubled from 1978 to 1988. The disease structure has changed in China. The cardio-cerebro-vascular diseases and cancer have become the leading causes of death in many cities. Recently we carried out an Inter-Health Programme in the East District of Beijing including a baseline survey, population intervention and disease monitoring. One hundred thousand people aged 15-75 selected for the survey were divided into experimental and reference groups. The morbidity, risk factors of common chronic diseases in the aged people (e.g. hypertension, stroke, coronary heart disease, cancer, diabetes and cataract) and the nutritional status were investigated.

The findings on nutritional survey in 869 inhabitants aged 35-74 years were as follows:

1. The energy intake in 49% of men and 41% of women accounted for 110% RDA;
2. Fat intake as percentage of total energy exceeded 30%;
3. Intakes of table salt and cholesterol were high;
4. Average serum cholesterol was high. Cholesterolaemia (>200 mg/dl) in men and women was 18.1% and 27.3% respectively; and
5. Lipid peroxidation products was higher in aged population.

To counter these risk factors, we conducted an intervention study in this district. The hypertensive patients were supervised, health education against smoking was carried out widely, decreasing salt intake, advising rational balanced diet, encouraging physical exercise, and emphasising the benefits of Chinese diet habits in order to improve the nutritional status in the elderly and to decrease the prevalence of common chronic diseases in China.

Proc 6th ACN 1991: 151-155

Nutritional status and aging factor analysis of Korean elderly

Sook He Kim

Department of Foods and Nutrition, Ewha Womans University, Seoul, Korea

Aging actually starts from the moment of conception; there is no exception among living organisms to aging. However, the aging process does not occur as a single definite process, but in a multifactorial process. There are two major factors which influence aging: one is genetic factor which is programmed within the cell and therefore, it is determined naturally, and the other factor involves the interaction with environmental and ecological influences. And by the later factor, one can observe individual difference of aging.

The average life expectancy of Korean population has increased in recent years owing to the country's remarkable economic progress.

In 1960s, Korea was an underdeveloped country with a per capita GNP of under $1,000. The per capita GNP of $1,000 was reached in 1976, and this made Korea one of the developing countries. From 1976 to 1985, per capita GNP rose to $2,000. The Economic Planning Board has now announced that the current per capita GNP has reached $5,000. Owing to the marked economic growth in the past 25 years, the health status and dietary pattern have been altered nationwide.

With economic changes along with dietary changes, the average life span of Korean population was extended greatly. In 1920s, the average life span of both men and women was only 23 years and life span difference between male and female was only 2-3 years. Recent data on life span in 1990s show that male has an average life expectancy of 66, and female has 74, and this makes a 8- year difference in life expectancy between two sexes. The substantial improvement of life expectancy up to 70 years has increased the proportion of old population.

We can clearly observe that the population demography has changed greatly with economic improvement. The population of over 65 yr old comprised 3.8 % in 1980, 4.2 % in 1985, and will increase to 6.2% in the year 2000, which will be doubled from the present.

The dietary surveys of elderly people conducted by various researchers show that the total food consumed by old people over 70 yr was 10-30 % less compared to the national average consumption. Especially, rural women consumed extremely small amounts of food viz. 780 g/person/day.

A dietary survey of May-June, 1990 on 217 elderly people from rural (121) and city areas (196) by a 24-hr recall method showed that subjects from the city consumed a greater amount of animal foods such as meat, fish, shellfish, milks and dairy products. Also subjects in cities consumed more vegetable, fruit, Kinchi, beans and seaweeds. Fat and oil consumption was higher in city elderly. However, the

rural elderly consumed the grain and cereals more than in cities. It is interesting to notice gender and regional differences of food consumption pattern of elderly in Korea (Table 1).

TABLE 1

Regional comparison of mean consumption of different food groups

Food Group	Mean consumption (g)			
	Urban		Rural	
	Male	Female	Male	Female
Animal food	253.6	204.4	113.7	68.8
Plant food	941.3	903.8	717.3	700.6
Fats & oils	13.4	14.2	3.0	3.0
Alcohol	4.8	3.4	148.0	8.9
Total	1213.1	1152.8	982.0	781.3

The city elderly consumed all the nutrients except carbohydrates (CHO) at a higher level - energy, protein, fat, calcium, some vitamins and some minerals. The CHO intake was higher in the rural elderly. The proportion of CHO for energy among the three major nutrients were 65% for city subjects and 80% for rural subjects. The proportion of protein and fat for total energy was smaller in rural elderly (Table 2).

There were no differences in energy intakes per kg body weight in both city and rural elderly.

The blood pressure measurement of Korean elderly subjects showed that the mean systolic pressure of males aged 60-69 were 117-131 mm Hg, and 131-125 mm Hg for females between the age of 60-69. After 70 years, the systolic and diastolic pressures of females were slightly decreased until mid-70s and increased afterward. But for males, the continuous increasing pattern of systolic pressure was observed up to 149 mm Hg in elderly over 80. The average diastolic pressure of male subjects showed the increasing tendency with age; it increased from 65 mm Hg in 60-69 yr olds to 90 mm Hg in 80 yr olds.

The blood profile of 23 healthy rural subjects between the ages of 70-93 was compared to 11 controls within the ages of 22-27. The average triglyceride (TG) level was 149 mg/dl for elderly subjects and 86 mg/dl for controls. The serum cholesterol was 222 mg/dl for elderly and 172 mg/dl for controls. HDL-cholesterol level was 46 mg/dl for elderly and 52 mg/dl for controls. LDL-cholesterol level was 148 mg/dl for elderly and 103 mg/dl for controls. Blood lipid compostion has increasing tendency with age.

The anaemia prevalence of elderly people in small and medium size cities varied according to the criteria applied to assess the anaemic condition. The average iron intakes of 16 mg and 17 mg were found for city females and males respectively, showing a large gap in iron intakes between city elderly and rural elderly in both sexes (8.8 mg for females and 10.1 mg for males).

The haematologic and serum iron values of elderly over 65 in males and females with normal ranges of values

TABLE 2

Regional comparison of daily nutrient consumption in elderly Koreans

Nutrient / Sex	Region	Calories (kcal)	Protein (g)	Fat (g)	CHO (g)	Ca (mg)	Fe (mg)	Vit A (R.E.)	Vit B1 (mg)	Vit B2 (mg)	Niacin (mg)	Vit C (mg)
Male	Urban	1904.9[1]	87.4	35.2	307.7	816.6	16.9	767.0	1.3	1.5	34.0	108.9
	(N=23)	± 489.5	± 33.3	± 16.0	± 72.8	± 463.5	± 6.6	± 427.5	± 0.6	± 0.4	± 18.6	± 54.1
		(100.3)[2]	(124.8)	-	-	(136.1)	(169.0)	(109.6)	(130.0)	(125.0)	(262.3)	(198.0)
	Rural	1672.1	55.9	14.5	311.2	403.1	10.7	440.3	0.8	1.0	16.0	65.8
	(N=29)	± 523.2	± 23.3	± 12.1	± 86.2	± 224.9	± 5.9	± 552.9	± 0.3	± 1.0	± 11.1	± 58.8
		(88.0)	(79.8)	-	-	(67.2)	(107.0)	(62.9)	(80.0)	(91.7)	(124.8)	(119.6)
		*	***	***	***	***	*	**	***	**		
Female	Urban	1724.7	75.2	33.4	280.8	781.8	16.1	755.1	1.2	1.3	28.0	116.7
	(N=98)	± 380.2	± 25.7	± 17.1	± 64.4	± 322.1	± 6.2	± 452.2	± 0.8	± 0.4	± 14.6	± 57.5
		(107.8)	(122.5)	-	-	(130.3)	(162.0)	(107.8)	(120.0)	(116.7)	(215.4)	(212.4)
	Rural	1530.9	47.4	11.1	307.0	373.4	8.8	381.4	0.7	0.6	11.9	54.3
	(N=67)	± 465.0	± 21.0	± 9.4	± 88.8	± 277.6	± 6.7	± 369.1	± 0.5	± 0.3	± 9.1	± 33.5
		(95.7)	(79.2)	-	-	(62.2)	(88.0)	(54.5)	(70.0)	(58.3)	(91.5)	(98.9)
		**	***	***	*	***	***	***	***	***	***	***

1 Mean ± SD

2 Percent of RDA

* Significant at p = 0.05 by t-test between urban and rural aged

** Significant at p = 0.01 by t-test between urban and rural aged

*** Significant at p = 0.001 by t-test between urban and rural aged

were investigated.

Hb, Haematocrit, MCHC, serum iron (SI), total iron binding capacity (TIBC) and transferrin saturation percent (TS%) values were distributed within normal ranges with exception of TS% in both sexes and SI value in female which was lower than normal values (Table 3). From 5.6% to 22.2% of elderly men and from 5% of elderly women were found to be anaemic according to the different criteria of assessment.

TABLE 3
Haematological and serum iron values of elderly in Korean males

	Mean	Normal Distribtion
Hb (g/dl)	15.2	13 -
Hct (%)	43.6	42 - 52
MCHC (%)	34.8	32 - 36
Sl (μg/dl)	59.2	80 - 180
TIBC (μg/dl)	327.6	280 - 400
TS (%)	19.4	20 - 50

Source: John-Hee and Myong-Wha Shin, Nutritional Status
In Healthy Elderly Koreans from Urban Households. Korean J Nutr 1988; 21:12.

The bone density studies of elderly over 50 showed that subjects experienced one or more bone fractures had lower bone density, and calcium intakes were lower in these subjects (Table 4).

The age of appearance of aging symptoms such as memory loss, poor eyesight, loss of hearing, graying hair, wearing dentures, was examined in 217 city and rural subjects. In most of subjects, the loss of memory started in their 50s. Those subjects who still possesed good memory after 70 years of age were found more among female elderly.

Subjects responded that poor eyesight began in their 40s for females and 50s in males. The poor hearing started in 60s for both sexes, and gray hair began to appear in their 40s for females and 50s for males. The age of wearing dentures were 30s for females and 40s for males. The neuromuscular aches started at 30s for females and 60s for males. The feeling of senility started in 50s in both sexes (Table 5).

The recent multiple stepwise regression analysis of 217 subjects by Ewha Women University between the aging and the contributing variables, such as health, socioeconomic status, daily activities, social participation, calorie intakes and behavior pattern showed that increasing age was correlated with excellent health, region-rural areas, bone and tooth health.

The multiple stepwise regression equation developed is as follows:

TABLE 4
Comparison of bone mineral density (BMD) between normal and fracture- experienced elderly subject

Age (year)	51 - 60		61 - 70	
BMD (g/cm^2)	FE	N	FE	
Spine	0.83±0.049	1.02±0.170	0.75±0.093	1.08±0.117
Femur neck	0.68±0.510	0.80±0.073	0.56±0.073	0.83±0.093
Wards triangle	0.54±0.041	0.66±0.065	0.39±0.074	0.06±0.092
Trochander	0.57±0.053	0.69±0.068	0.45±0.058	0.71±0.100
Ca intake (mg)	421±129.4	673±130.9	479±135.4	640±169.6

FE: fracture-experienced, N: normal subject

Source: Choi Eun Jeong. A study on correlations between national states physical activity and bone mineral density in postmenapausal women, 1988.

TABLE 5
Self-recognised aging symptoms by age group*

Symptom	Sex	Age group (yrs) 30-39	40-49	50-59	60-69	> 70	Good**
Memory decreased							
	M	0***	1	8	22	13	8
	F	0	6	27	51	56	25
Eyesight decreased							
	M	1	1	13	20	8	6
	F	0	14	29	54	37	31
Hearing decreased							
	M	1	0	3	9	9	30
	F	1	2	12	29	53	58
Grey hair appearance							
	M	1	7	14	22	8	0
	F	1	46	48	45	21	4
Half denture							
	M	0	2	9	18	8	15
	F	4	7	21	72	31	30
Feeling of senility							
	M	0	0	6	26	16	4
	F	0	4	23	83	47	8
Neuro-arthritis							
	M	2	1	6	19	8	16
	F	10	17	36	41	31	30

* Males = 52, females = 165 ** Not recognised at present
*** Units refer to numbers

$$Y = 12.68 + 0.13HS\ 2.76RE + 0.11BT - 0.13SES + 0.05ADL - 0.07SP - 0.0003Cal - 0.02BP.$$

(HS: health status, RE: region, BT: bone & tooth health status, SES: socioeconomic status, ADL: activities of daily living, SP: social participation, Cal: Calorie, BP: behavior pattern).

References

1. Chung CE, Kim SH. Effects of nutritional status of the elderly Korean on aging process. Kor J Gerontol 1991; 1 (1): 98-106.
2. Chung CE, Kim SH. A study on the statistical analysis of aging factors on elderly Korean. Kor J Gerontol 1991; 1 (1):107-113.
3. Survey for elderly nutritional status. Food Research Institute, Seoul, Korea, 1987.
4. Han SS, Kim SH. Nutrition consumption status in relation to bone density in Korean elderly. Kor J Nutr 1988; 21(5):333.

Proc 6th ACN 1991: 156-159

Dietary habits and nutritional problems of the elderly in Japan

Yoshiaki Fujita and Hidemichi Ebisawa

Department of Nutrition, Division of Physiological Aging Research, Tokyo Metropolitan Institute of Gerontology, Tokyo, Japan

Introduction

Scientifically reliable data indicate that the maximum life span of human beings seems to be in the range of 110 to 120 years. However, the mean life expectancy at the present time is far from the maximum life span, because we are usually exposed to various external factors which shorten longevity. Of the external factors, dietary and nutritional conditions relate directly to health and the appearance and development of some diseases. This has an uncompromising effect on specific life expectancy.

Changes in leading causes of death

Japan is moving towards an advanced-age society at a very high speed. In 1990, the mean life expectancy of Japanese was 75.86 years for males and 81.81 for females. The percentage of elderly (those over 65 years old) in the population was over 12%. Statistical data indicate that by the year 2020, one of every four Japanese will be at least 65 years old. The major factors which have extended the mean life expectancy of Japanese are the developments in scientific technology, particularly medical technology, the successful control and improvements in environmental sanitation and nutritional status.

After the Second World War, western habits penetrated Japanese life to an enormous extent. In addition, the socioeconomic developments during the last two decades have changed the lifestyle of people and accelerated the westernising of dietary and eating habits. Particularly, a noteworthy increase in the intake of animal foods has greatly improved the nutritional status of people who were undernourished after the Second World War.

In the past, when most Japanese had inadequate nutritional status, undernutrition-induced infectious diseases such as tuberculosis and other communicable diseases constituted the major causes of death of Japanese people. However, with changes in dietary and eating habits, the incidence of such diseases declined and then overnutrition-induced degenerative diseases such as malignant neoplasms, heart disease, and cerebrovascular disease took over as the leading causes of death (1).

However, it is important to note that the age-adjusted mortality rates, in which the population composition is expressed on an equalised age-distribution basis, show that those suffering from the chronic degenerative diseases have remained almost constant during the last three decades.

The present leading causes of death as expressed by age groups are malignant neoplasms, heart disease and cerebrovascular disease. These are followed by suicides and accidents for the middle-aged, followed by undernutrition-induced infectious diseases for

the elderly population. This suggests that among the elderly, not only overnutrition but also undernutrition is a serious problem that needs to be addressed.

Food preferences and related factors

Japanese elderly persons have a preference for foods coming from the traditional Japanese dishes rather than western foods. Moreover, they preferred dishes made with the best natural ingredients rather than highly processed foodstuffs. Results from the National Nutrition Survey showed that the mean daily intake of vegetable foods increased with age for the head of a family, while the daily intakes of fats and oils, milk and dairy products and meats decreased (2). Although age-related changes occur in the pattern of foods consumed, the daily nutrients intake satisfied the Recommended Dietary Allowance (RDAs), irrespective of age and nutrition (2). This suggests that as long as people have diets with an adequate variety of foods, differences in food patterns are not nutritionally disadvantageous.

There is no conclusive evidence to suggest any characteristic food preferences in the elderly result from the aging process or an adaptation to changes in the living environment. Suyama *et al.* (3) examined 422 elderly men and women, aged 69-71 years old living in an urban area and found that the three leading factors determining the number and variety of foods consumed were: level of education, level of activity of daily living (ADL) and the type of living arrangements.

Furthermore, Uchino (4-5) showed that the frequency of rice-oriented dishes among three meals a day, which has been generally thought to be more common for Japanese elderly persons, was strongly influenced by differences in residential location, kind of occupation, level of education and social position rather than differences in age. These findings suggest that characteristic food preferences and eating habits among elderly persons depend strongly on changes in their socioeconomic environment rather than on age-related changes in physiological functions.

Nutritional status

Results from the recent National Nutrition Survey (2) showed that the nation's mean nutrients intake comes close to expectations. The rates of energy derived from proteins (P), fats (F) and carbohydrates (C) in a conventional Japanese diet were 15.2%, 24.5% and 60.3%, respectively, of the dietary energy ingested (2). These ratios, for the habitual diet are comparable to that for "the Dietary Goal". However, it should be noted that the average value encompasses large deviations from under-to over-consumption.

In the elderly, levels of ADL reflect well their nutritional status. Among aged persons, there is a group, the "immobile-elderly" such as housebound and/or bedridden elderly persons who have low levels of the ADL. In these elderly persons, deficiencies in the intakes of some nutrients, particularly vitamin A, vitamin B2, calcium and iron, have been common (6-7). Another group is the "dynamic-elderly" who take an active part in a company, community, or household affairs. Elderly persons from this group have generally good nutritional status (8-10).

However, the nutritional status of institutionalised elderly persons lies generally between the "immobile-elderly" and the "dynamic-elderly". In institutions and homes for the elderly, in general, the mean eating rates of elderly persons are not as high as those of household elderly, resulting in decreased intakes of nutrients. This is because in most institutions a uniform

meal is served to all residents who may have differences in eating habits, dietary customs, and food preferences (8).

Nutrition evaluation

The RDAs for children and young adults are based on theory but confirmed scientifically by many experimental data (11). However, most of the RDAs for Japanese elderly persons have been estimated in accordance with those for young adults, because of the paucity of data available.

Ishigaki *et al.* (12) found that the daily energy intake of elderly persons was below their RDAs, but conformed well with their daily energy expenditures. Most Japanese elderly have eating habits that begin with eating rice at every meal. Rice is considered to be the staple food and the main energy source. In the elderly who have less daily energy needs, this eating habit results in decreased ingestion of other foods rich in protein, vitamins, and minerals. The solution to this problem would be to encourage the habit of beginning meals with dishes other than rice.

Physiological functions

Taste sensitivity for sweet, sour, salted and bitter foods decrease steadily with advancing age. Undoubtedly, a matter of great importance in food services for the elderly is the consideration for balanced nutrition, inter-individual differences in physiological functions and appetite enhancement. Accordingly, we must take into account taste, odour, texture, colour of foods, materials, their colour, size, shape of tableware, and dishes. All are relevant factors for the promotion of appetite.

Drug and nutrition

The use of prescription drugs for chronic age-associated diseases is more common in elderly persons. However, certain prescription drugs cause malabsorption of some nutrients, particularly vitamins and minerals, and an abnormal metabolism and utilisation of certain nutrients. Further, drugs may impair the functioning of some organs, resulting in malnutrition (13). For nutrition control in the elderly, it is very important to consider what sort of medical drugs he/she normally uses.

Psychological change and nutrition improvement

Spiritual faith is essential for a healthy and meaningful elderly life. But decreases in psychological pliability and emotional control increases social isolation and loneliness. These are quite common in elderly persons. "Nothing to worry about diet", "can have any kind of foods in any amount whenever he or she wants to eat" and "having a good appetite for every meal", are undoubtedly positive attitudes that bring spiritual happiness and satisfaction to elderly persons. Accordingly, efforts to cultivate these responses are prerequisite steps for improving the nutritional status of elderly persons.

References

1. Data Book of Food, Nutrition & Health 1991, 11th Edition. Tokyo: Ishiyaku-Syuppan, 1991 (in Jpn).
2. The Present Nutritional Status of Japanese (Result of National Nutrition Survey, 1989). Ministry of Health & welfare (ed). Tokyo: Daiichi-Syuppan, 1991 (in Jpn).
3. Suyama *et al.* Ronen-Syakai-Kagaku 1984; 6:197-210 (in Jpn).
4. Uchino S. Jinko-Mondai-Kenkyu (The Journal of Population Prob-

lems) 1980; 156:15-38 (in Jpn).

5. Uchino S. Jinko-Mondai-Kenkyu (The Journal of Population Problems) 1981; 160: 1-22 (in Jpn).
6. Okumura *et al.* Rinsyo-Eiyo (Jpn J Clin Nutr) 1980; 57: 271-278 (in Jpn).
7. Yoshida S. Abstracts of Papers, the 41st Annual Meeting of the Japan Dietetics Society 1987, pp. 123 (in Jpn).
8. National Institute of Nutrition: Report on Studies on Development of Indices to Assess Health and Nutritional Status for Older Adults, 1985 (in Jpn).
9. Adachi *et al.* Abstracts of Papers, 40th Annual Meeting of the the Japan Society of Nutrition and Food Science 1986, p. 125 (in Jpn).
10. Matsudaira *et al.* J Kyoto Med Assoc 1987; 34:55-63 (in Jpn).
11. Recommended Dietary Allowances in Japan, 4th Edition. Ministry of Health & Welfare (ed). Tokyo: Daiichi-Syuppan, 1984.
12. Ishigaki *et al.* Jpn J Nutr 1976; 34:71-76 (in Jpn).
13. Roe DA In: Geriatric Nutrition, 2nd Edition, pp. 176-200. New Jersey: Prentice-Hall Inc., 1987.

Proc 6th ACN 1991: 160-164

Warning signals for malnutrition in the elderly: A global perspective

Louise Davies

Gerontology Nutrition, Royal Free Hospital School of Medicine, London NW3 2QE, United Kingdom

Introduction

This century has witnessed an unprecedented rise in numbers of men and women surviving to old age, although the definition and the perception of `elderly' may vary in cultures with differing life expectancies.

In countries where food supplies are sufficient, the majority of old people can maintain adequate nutritional status even into extreme old age (1). There is also a recognised group that reaches advanced old age as `elderly elite' with physical and mental vigour.

However for others, advancing age may bring an interplay between disease, physical and/or mental disability, environmental, economic and social difficulties. These combined forces can exceed an elderly individual's reserve capacity, i.e. the ability to respond to stressors (2) and can lead to a debilitated state or a downward spiral in health. Thus, elderly individuals are particularly susceptible to malnutrition and sub-clinical malnutrition may be common (3-7). Age associated nutritional problems are expected to result in escalating demands on already overstretched medical and social services.

Those responsible for the first large-scale British government nutrition survey of the elderly observed in their report that, in some at least of the old people studied, malnutrition might have been prevented if the hazards had been recognised and the appropriate community services deployed (8).

In a follow-up report, and numerous studies in other countries, risk factors for malnutrition in elderly populations have been identified (9-10).

Risk factors and warning signals

Based on a previous definition relating to children (11): **a risk factor is a major, identifiable biological or environmental circumstance or event that increases the risk of malnutrition and therefore suggests the need for special care and attention.**

However, the recognition of risk factors does not necessarily target those individuals most in need. There is rarely a direct cause-effect relationship. For example, being housebound is a recognised risk factor (1), but it certainly cannot be assumed that all housebound elderly people are malnourished.

Following the previous definition of risk factors, **warning signals are single, or groups of, observable circumstances that, if left unchecked, might directly cause an `at risk' individual to become malnourished.**

It is evident that malnourishment of a housebound old person becomes more likely if there are accompanying observable warning signals such as `insufficient food stores at home' or

observed `depression/loneliness'.

Identification of risk factors specific to each country makes it possible to target groups who may be especially susceptible to malnourishment, or may indeed already be malnourished. Thus, priorities for action could be established, together with appropriate policies. However, it is acknowledged that `the elderly' can be the most neglected sector of the population with reference to government programmes, and the most forgotten by society.

When national disasters such as floods or earthquakes occur, priority is given to emergency political action; other risk factors, such as unsanitary water supplies, may call for high level public health measures. Elderly people are particularly vulnerable to these risks, and often either fail to survive or have to be left behind as more mobile family or neighbours leave the area.

However, it must be realised that even seemingly minor concerns may become a disaster to an elderly individual, regardless of country of origin. Thus, living alone can swiftly result in malnutrition if the old person is left unable to fend for him/herself. The resultant warning signal `isolation' may have different causes in different cultures, e.g. left alone whilst the family works in the fields; left alone at the top of a high rise block of flats, unable to reach the food stalls below; left alone in the city when the family takes the traditional long summer holiday; left alone without visitors when a favourite grandchild goes to university.

With the realisation that those most in touch with elderly people may be their neighbors, friends or relatives, a community based approach to the prevention of malnutrition has been developed (12). Its aim is to teach the recognition of the relevant warning signals to the health workers and care providers, including the lay public, with practical steps for simple intervention at 'grass roots' level.

A clear form, drawn up in a grid system, can be filled in by such `field workers' for later reporting and assessment back at base (Figure 1). The most commonly found warning signals under each risk factor are marked in the grid of Figure 1 with an asterik (*).

To clarify the concept, this figure has been marked-in to illustrate the case of a hypothetical elderly person (who may be e.g. of low socio-economic status, living alone and ill - these risks are ticked by the field workers). The grid has been further marked with circles to indicate the warning signals that may have been observed in this case.

Thus it can be seen at a glance that low socio-economic status might result in a low budget for food (some people with a low income may economise on other expenses but are still able to put aside enough money for their nutritional requirements, so this needs to be checked, possibly by observing insufficient food stores and long periods in the day without meals, snacks or fluids). This may have resulted in an observed unexplained change in weight. These warning signals could also have been the result of living alone: indicated by observed physical disability, isolation and insufficient nutritional knowledge to make food choice. Illness could further exacerbate the risk of malnutrition; indeed, if vitamin A deficienty is suspected, a further warning signal of "falling over" may need to be added to the grid, to support a possible diagnosis of nigh blindness.

In the British government study (9) it was found that the likelihood of malnutrition in an individual increases with a multiplicity of risk factors: thus the warning signal `recent unintended weight change' assumes even greater urgency for various forms of practical preventive action if it is associated with more than one risk factor. Those indi-

Examples of risk factors and observable warning signals

Check for warning signals under each risk factor
* = most likely

Warning signals	Low socio-economic status ✓	Housebound/living alone ✓	Nourishing food unavailable/expensive	Insanitary water supplies/pollution	Disaster: e.g. floods	Lack of community food programs	Disease: e.g. diabetes/bowel disorders ✓	Poor dentition and/or difficulty in swallowing
Recent unintended weight change±3kg (7lb)	⊛	⊛	*	*	*	*	⊛	*
Physical disability affecting food procurement, preparation or intake		⊛			*	*	*	*
Isolation		⊛			*	*		
Bereavement and/or observed depression/loneliness		*			*	*		
Mental confusion affecting eating		*			*		*	*
High alcohol consumption	*	*		*			*	
Long term medication or lack of appropriate medicines	*	*		*	*		⊛	
Missed meals/snacks/fluids	⊛	⊛	*	*	*	*	*	*
Lack of work capacity	*	*			*	*	*	
Insufficient food stores at home	⊛	⊛	*		*	*		
Poor food hygiene		*		*	*		*	
Low budget for food	⊛	*	*		*	*		
Needing nutritional knowledge	*	⊛	*			*	⊛	*

viduals with 4 or more risk factors were at considerable risk of malnourishment, with medical conditions playing an important role. Under the heading of `disease', it is therefore important to identify the chief medical risks to elderly men and women in each country.

Following recognition of the interacting problems, the type of `first aid' practical actions for the prevention of nutritional crisis are seen as simple, informal and inexpensive, varying with the needs and wishes of the individual, e.g. help with procurement and preparation of food, help with the physical difficulties of feeding, or even something non-nutritional such as help with a walking aid to stimulate independence.

The encouragement of this community-based approach in no way disregards the more structured care of the social and health services that may already exist. On the contrary, the lay person's observations frequently highlight the need for medical or paramedical services; or the urgency of the introduction to a total package of care, including meals programs or other community services.

Implementation

The first step is to identify the risk factors and warning signals relevant to each country, including separate cultures or religions within the country. At past International congresses of nutrition a poster has been displayed to encourage delegates to identify/add risk factors and warning signals relevant to their country. Some examples have been given in Figure 1. They are open to discussion, with suggestions for additions or deletions, at this Congress.

Who can implement?

The dietitian's role as the nutrition expert makes him/her particularly suited to educate the medical and paramedical profession and the lay public on risk factors and warning signals. In countries where there are few dietitians, this role could be taken by nurses, social workers or other community health workers.

The help available to them will vary: there may already be professional groups or individuals concerned with the welfare of elderly people, and they might be persuaded to become involved with the unformal care and with follow-up assessments. A checklist leaflet of support services locally available may need to be written to help the carers to take the necessary, appropriate, prompt action, informal meetings can help to explain and distribute this check list. It may be possible to involve the media: local newspapers, poster campaigns, radio or television could all help to educate lay people on the warning signals and where to find supportive services.

When is it necessary to implement a preventive approach?

There are four types of malnutrition that may make the elderly particularly vulnerable at various periods of their life:

Specific malnutrition (e.g. diabetes) sometimes masked by non-nutritional disease, calls for skilled, early diagnosis and clear dietary instructions for patient and carer.

Recurrent malnutrition needs long-term planning for services in the community.

Sudden malnutrition (e.g. following surgery or bereavement) calls for prompt assistance to encourage regaining of appetite.

Long-standing malnutrition calls for the front-line carers to initiate action as early as possible to prevent a crisis.

The implementation of appropriate "first aid" action might help to prevent a downward spiral and assist elderly people to remain independent for as long as possible. The aim is improved health for all, but with special help for those at greatest nutritional risk.

References

1. Exton-Smith AN. Nutritional status: diagnosis and prevention of malnutrition. In: Exton-Smith, AN and Caird, FI. Metabolic and Nutritional Disorders in the Elderly. Bristol: John Wright and Sons Ltd., 1980.
2. Chernoff R. Aging and Nutrition. Nutrition Today 1987; 22 (2): 4.
3. Worthington-Roberts BS and Hazzard WR. Nutrition and aging.

In: Eisdorfer C (ed), Annual Reviews of Gerontology and Geriatrics 1982; 3: 297.

4. Yeung DL, Scythes CA, Zimmerman SA, Pennell MD. Nutrition of Canadians 65 years and over - a review. Can J Public Health 1986; 77: 363.
5. Morley JE. Nutritional status of the elderly. Am J Med 1986; 81: 679.
6. Cashman MD and Wightkin WT. Geriatric malnutrition: recognition and prevention. Compr Ther 1987; 13: 45.
7. Vir SC and Love AHG. Nutritional status of institutionalised and noninstitutionalised aged in Belfast, Northern Ireland. Am J Clin Nutr 1979; 32: 1934.
8. Department of Health and Social Security (DHSS). A Nutrition Survey of the Elderly. Report on Health and Social Subjects No. 3. London: Her Majesty's Stationery Office (HMSO), 1972.
9. DHSS Nutrition and Health in Old Age. Report on Health and Social Subjects No. 16. London: HMSO, 1979.
10. Davies L. Socioeconomic psychological and educational aspects of nutrition in old age. Age and Ageing 1990; 19: S37-42.
11. Bindary A, Hutchings JJ, Jelliffe D, Gabr M. Guidelines on the at risk concept and the health and nutrition of young children. Am J Clin Nutr 1977; 30: 242.
12. Davies L and Knutson KC. Warning signals for malnutrition in the elderly. J Am Diet Assoc (in press).

Proc 6th ACN 1991: 165-171

Dietary patterns of the elderly: theoretical considerations - culture, diet and nutritional status

[1]Wahiqvist ML, [1]Kouris-Blazos A, [2]Trichopoulos A, [3]Sun MT, [3]Xi S, [1]Lo CS, [1]Hage B, [4]Gracey M, [4]Sullivan H

[1]Department of Medicine, Monash University, Prince Henry's Hospital, Melbourne, Australia; [2]Department of Nutrition & Biochemistry, Athens School of Public Health, Athens, Greece; [3]Division of Geriatric Nutrition, Institute of Hygiene, Tianjin, China; [4]Aboriginal Health Unit, Health Department of Western Australia, Perth, Australia

Introduction

Later life is characterised by great heterogeneity from the point of view of biological age and, therefore, potentially, food and nutrients needs. In turn, this heterogeneity and the extent of it, may reflect life-long and current food habits. The International Union of Nutritional Sciences (IUNS) "Food Habits in Later Life" project seek to assess how much of the variance in health status in later life can be accounted for by food habits and the extent to which altogether culturally disparate food habits might be associated with comparable levels of health. Communities under study include those in the place to which their culture belongs (e.g. Greeks in Greece, Chinese in China, Aboriginal Australian in Australia), and people out of cultural context (Greeks, Chinese and Anglo-Celtics in Australia, dislocated indigenous peoples in their country). Such studies allow an appreciation of food, cultural, and health resilience or susceptibility. For example it is possible to test whether there is an environmental effect or whether there is evidence of genetic (ethnic) differences in the development of cardiovascular risk in the same environment.

Elderly Greeks in Greece and Australia, Chinese in China & Australia, Anglo-Celtic & Aboriginal Australians

Major causes of death

According to 1981 mortality rates (1) Greek Australians live longer than native born Australians and Greeks in Greece, making them the 2nd longest lived population in the world (Japanese in Hawaii being the first) (2). Greeks in Greece aged over 75 have low death rates from heart disease and cancer, but high rates of stroke and diabetes (1986 WHO). In 1982, Greek Australians aged over 65 maintained their low death rates of heart disease and cancer (although rates are on the increase, especially colonic and breast cancer with increasing length of stay (3), and in the new environment death rates from stroke had dropped. Chinese in China are similar to Greeks in Greece in that they also have low death rates of heart disease and high rates of stroke, the difference being the much higher rates of cancer in China (1988 Encyclopedia Britanica). In 1982, Asian Australians aged over 65 showed a marked increase in heart disease death

rates but a drop in stroke and cancer rates in the new environment (1). Compared to both Greek and Asian Australians, Anglo-Celtic Australians aged over 65 have slightly higher dealth rates from stroke and cancer, almost twice the death rates from heart disease compared to Greek Australians, but equivalent rates to Asian Australians (1). Compared to non-Aboriginal Australians, Aboriginal Australians have a lower life expectancy by about 20 years, have twice the rates of circulatory diseases and have one of the highest reported incidences of diabetes in the world (4).

Food patterns

Comparing intake of various foods by different cultures may provide some insight into country/culture specific disease patterns. So far, in the IUNS study, 104 (51 men, 53 women) Greeks in Greece aged over 70, 440 (209 men, 231 women) Chinese in Northern China (Tianjin) aged over 70, 54 (23 men, 31 women) Aboriginal Australians aged over 50 (upper decile of population), have been studied and programmes near completion include 200 Greeks and 200 Anglo-Celtic Australians and 200 Swedes in Sweden. The food intake data from Greece and China will therefore be compared to existing data from the Victorian Nutrition Survey conducted in 1985 on 2935 people, of which 525 were aged over 60 (239 men 286 women) (5). Although the food intake instrument used in the IUNS study was slightly different and the sample is aged over 70, it still allows one to observe crude difference in food intake (Table 1). The most striking differences are in the low intake of meat, fruit and dairy products, and high intake of cereal foods of the Chinese where as Greeks appeared to have a higher intake of most foods, especially fish, meat, legumes, cheese,

TABLE 1
Mean daily consumption (grams) of foods for Australians aged over 60 years (1985) and for Greeks and Chinese aged over 70 years (1988)

	AUSTRALIA Victorian Nutrition Survey 1985(5)		GREECE IUNS 1988 (6)		CHINA IUNS 1988 (7)	
FOOD g/day	Men n= 239	Women n= 286	Men n= 51	Women n= 53	Men n= 209	Women n=231
Meat	36	29	43	34	25	24
Fish	14	11	42	34	13	7
Egg	17	12	15	12	17	8
Cheese	18	20	63	42	0	0
Milk	241	256	94	107	5	5
Yoghurt	10	22	32	35	0	0
Cereal	196	154	252	170	350	310
Vegetables	253	303	324	244	215	183
Legumes	23	3	33	31	20	13
Fruit	151	213	196	170	10	9
Plant oil	NA	NA	52	39	23	20
Lard	NA	NA	0	0	6.5	5.5

yoghurt and plant oil (mainly olive oil). The Anglo-Celtic Australian diet, although high in vegetables and fruits, is low in cereal foods. Minimal plant oil is used by Anglo-Celtic Australians, margarine being preferred as a spread on bread and for cooking. Both Chinese and Greeks do not use margarine, plant oils are mainly used for cooking and lard is also used in cooking by the Chinese.

According to the 1984 Australian Household Expenditure Survey, migrants from both Greece and Asia displayed a marked increase in expenditure on meat (which for migrant Greeks was even higher than Australian born), as well as milk, margarine and fruit (especially by Asians). These changes however have occurred against a background of continued high vegetable and cereal intakes, as well as fish and use of plant oils (8).

There are appreciable differences in food sources between the 3 countries. Vegetable intake of Greeks is characterised by tomatoes, onion, capsicum, and leafy greens (endives), where as for the Northern Chinese it is characterised by corn, bean shoots, Chinese cabbage and sweet potato and for the Anglo-Celtics by potatoes, peas, green beans and carrots. Cereal intake of Greeks is mainly supplied by wheat as bread and pasta, where as for the Northern Chinese it is mainly rice as well as wheat (which is plentiful in the North but not the South) in the form of steamed buns and noodles. Anglo-Celtic Australians (especially the elderly) mainly eat wheat as bread and breakfast cereals with limited intake of pasta and rice.

Aboriginal Australians

The food quality of the Aboriginal Australians studied was closely connected to the weekly payment of the pension ($Aust 100/week) whereby most food was purchased and eaten within 3 days of receiving their cheque which would be followed by minimal food for the remainder of the week. Such a food pattern could be due to a number of factors: (a) a natural inclination of feast-famine; (b) inadequate budgeting skills; (c) food is eaten and all the money is spent before it may be used by relatives or neighbours to purchase alcohol (excessive alcohol intake is in evidence in this community); (d) limited storage and refrigeration facilities. The main types of foods consumed on the plentiful days included: white damper (wheat flour and water mixture fried in oil or cooked in ashes), tinned corned beef, fried eggs, stewed lamb chops, take away chicken and potato chips, boiled potatoes, onions and minimal green vegetables, jam, sugar, tea, milk powder, minimal margarine. On other days only damper, tinned corned beef, tinned spaghetti and tea was consumed. Indigenous bush foods comprised less than 20% of total food intake (9).

About 50% of total energy is provided by sugar, beef, white flour and most of the fat is saturated fat from fatty cuts of meat. Nutrients that did not reach 70% of the RDI included Mg, Zn, folate, Ca, K, B6. Sodium intake was found to be 3 times the RDI, consumed mainly from the damper (Table 2).

The importance of food intake differences (as well as food sources and food distribution) between these cultures and changes upon migration or dislocation will be further investigated as data collection is completed in 1992. For example, of particular interest is the high cereal intake of the Chinese, the high fish, legume and plant oil intake of the Greeks, the high margarine and low cereal intake of the Anglo-Celtics, and the limited fruit and vegetable intake and very high intake of cereal (white flour) and sugar of Aboriginal Australians.

TABLE 2
Comparison of apparent intake of nutrients in aboriginal Australians and wider Australian communities

Nutrient	Wider Australian Community (10)	6 Remote Aboriginal Communities (11)	IUNS Aboriginal Australians (9)
Energy, kcal	3255	3663	4000
Protein, g	100	76.5	100
% energy	12	8	10
Fat, g	133	184	200
% energy	37	45	45
Total carbohydrate, g	398	453	450
% energy	49	50	45
Simple carbohydrate, g	124	250	200
% energy	15	27	20

Cardiovascular risk - serum lipids, body fatness and blood pressure

The following abbreviations have been given to the population groups for the purposes of comparison:

GG = Greeks in Greece, IUNS 1988, > 70 yrs

GA = Greeks in Australia, IUNS 1991 > 70 yrs

CC = Chinese in China, IUNS 1988, > 70 yrs

AC = Anglo-Celtic in Australia, IUNS 1988, > 70 yrs

AB = Aboriginals in Australia, IUNS 1988, > 50 yrs

CA = Chinese in Australia, 1989, > 70 yrs

Lipids

There were no statistically significant differences in lipids between the population groups studied. This suggests that cholesterol and triglyceride concentrations may be independant of environmental or genetic (ethnicity) influences in the aged population (Table 3).

Body fatness

The differences in body mass indices and waist hip ratios between the population groups studied, reached statistical significance ($p<0.0001$) (Table 4). Chinese in China and Australia had the lowest body mass indices and waist hip ratios and the Greeks in Australia had the highest. Nevertheless, compared to migrant Greeks, Asians in Australia have higher death rates from cardiovascular diseases.

Blood pressure

The differences in systolic ($p<0.0003$) and diastolic ($p<0.0013$) blood pressures between the population groups studied reached statistical significance (Table 5). Greeks in Greece and Chinese in Australia had the lowest diastolic blood pressure readings suggesting a possible genetic and

TABLE 3
Mean serum lipids for elderly Greeks in Greece & Australia, Chinese in Australia and Anglo-Celtic Australians*

	CHOL		TRIG		HDL		LDL		LDL/HDL	
	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women
GG, men=40 women=27	6.2	7.1	1.6	1.4	1.4	1.6	4.1	4.9	3.2	3.1
GA, men=44 women=34	6.1	6.3	1.3	1.3	1.3	1.5	4.2	4.2	3.5	3.0
CA**, men=11 women=9	5.8	5.8	1.9	1.4	1.3	1.3	3.7	3.9	3.0	3.0
AC, men=7 women=9	4.9	7.0	1.1	1.8	1.5	1.5	4.0	4.7	2.6	3.4

* mmol/l where appropriate
** Hage B, Wahlqvist ML, Oliver G, Balazs, N - Melbourne Chinese Health Study, unpublished data, 1989

TABLE 4
Mean body mass indices and waist hip ratios of elderly Greeks in Greece & Australia, Chinese in China & Australia, Anglo-Celtic & Aboriginal Australians

	BODY MASS INDEX (weight/height^2)		WAIST HIP RATIO (Umbilical/maximal gluteal circumferences)	
	Men	Women	Men	Women
GG, men=41 women=29	27	28	0.95	0.99
GA, men=69 women=76	27	29	0.97	1.02
CC, men=209 women=231	22	22	0.89	0.86
CA, men=11 women=8	23	22	0.95	0.94
AC, men=7 women=10	25	27	0.93	0.98
AB, men=20 women=22	23	27	0.98	0.97

TABLE 5
Mean systolic and diastolic blood pressure* of elderly Greeks in Greece & Australia, Chinese in China & Australia, and Anglo-Celtic Australians

	Systolic		Diastolic	
	Men	Women	Men	Women
GG, men=41 women=29	147	151	78	76
GA, men=89 women=75	154	154	82	83
CC, men=209 women=231	142	146	83	82
CA, men=11 women=9	143	139	77	70
AC, men=7 women=10	151	148	84	83

* Sphygmomanometer was used except for Chinese in Australia where a random zero device was utilised
Units: mm Hg

environmental interaction. Chinese in China and Australia had the lowest systolic blood pressure readings which implies a significant genetic influence.

One of the most significant changes in cardiovascular risk which occurs on migration is the higher waist hip ratio of both Greeks and Chinese in Australia where more fat appears to be distributed on the abdomen compared to the parent countries. However, the operation of fatness on cardiovascular risk (blood pressure and lipids) would appear to be differential in a health context which is similar for cardiovascular mortality. The IUNS data confirm that food culture needs description to account for differential risk and health profiles.

Linking food intake to cardiovascular risk and morbidity

There is considerable differential between ethnic groups in each of food intake, cardiovascular risk profile and cardiovascular morbidity. There appears to be both an interplay of environment and genetic factors in the expression of cardiovascular risk. However, it is difficult to discern one common sequence to link food intake to risk and then to mortality, other than by generation of broad categories. Therefore studies which explore this sequence cross-culturally allow the opportunity to discern more specific food-non food interactions in the determination of mortality profiles.

References

1. Department of immigration and Ethnic Affairs. Selection and Survival Mortality in Australia, Australian Government Publishing Service, Canberra, 1986.
2. Powles J, Gifford S. How Healthy are Australia's immigrants. In: The Health of Immigrant Australia. Harcourt Brau, in press, 1991.

3. McMichael AJ. Changes in Cancer Risk in Immigrant Australians. Proc Nutr Soc Aust 1983; 8: 41-8.

4. Gracey M, Spargo RM. The State of Health of Aborigines in the Kimberley Region. Med J Aust 1987; 146:200-4.

5. Baghurst K, Crawford D, Record S, Worsley A, Baghurst P, Syrette J. The Victorian Nutrition Survey, Part 1: Food intakes by Age, Sex and Area of Residence. CSIRO Division of Human Nutrition, Adelaide, SA, 1987.

6. Kouris A, Wahlqvist M. Nutrition and Ageing: Cross-Cultural Studies. In: Proceedings of 1st Australian Clinical Nutrition Conference. Australasian Clinical Nutrition Group, Royal Australian College of Physicians, May, Melbourne 1990.

7. Sun Ming-Tan, Xi Side. Division of Geriatric Nutrition, Institute of Hygiene, Tianjin, unpublished data, 1988.

8. Powles J, Hage B, Cosgrove M. Health Related Expenditure Patterns In Selected Migrant Groups: Data from the Australian Household Expenditure Survey. 1984. J Community Health Studies 1990; xiv: 1.

9. Wahlqvist ML, Kouris A, Gracey M, Sullivan H. An Anthropological Approach to the Study of Food and Health in an Indigenous Population. Food Nutr Bull 1991; 13 (2), United Nations University.

10. Australian Bureau of Statistics. Apparent Consumption of Food stuffs and Nutrients, Australia 1983-84. Canberra: Australian Government Printing Services, 1985.

11. Lee A. Apparent Consumption of Food and Nutrients in Coastal and Desert Aboriginal Communities: Implications for Nutrition Education. In: Proceedings of the Menzies Symposium "Nutrition and Health in the Tropics" Townsville, 270-288, 26-27 August, 1987: 270-288.

Proc 6th ACN 1991: 172-176

Nutritional situation of rural and urban elderly from selected East Asian and Latin American developing countries

Asri Rasad and Rainer Gross

SEAMEO-TROPMED Centre Indonesia, University of Indonesia and the Deutsche Gesellschaft fur Technische Zusammenarbeit GmbH (GTZ)

Introduction

Two of the major demographic phenomena of recent decades have been: (a) the growth of the elderly population (1,2); and (b) the growth of urban populations (3).

By the year 2020 the proportion of population over 55 years of age is due to increase by 72% in developing countries (1). From 1950 to 2000, the population living in cities in the Thirld World will have increased from 16.7% to 43.5%, a 2.6-fold increase (3).

The increase in the number of older people has stimulated interest in survey studies such as the Dutch study (4) and the incompletely published findings from the European Community Concerted Action on Nutrition and Health in the Elderly (EC-EURONUT-SENECA) project. However, it is not known to what extent the diet-disease relationships of developed countries (5) are modified by genetic and environmental factors present in Third World countries. Furthermore, the nutrient requirements and nutrient intake recommendations specifically for persons over 60 years of age are still not precisely defined (6). The gaps in our knowledge of the aging process and the health of the elderly in a developing region of the world such as Latin America are large (7). In developing countries, we only have a few examples of surveys of elderly populations such as the health and anthropometric survey in a suburban population in Coronado, Costa Rica (8) and the morbidity surveys in Korea, the Philippines, Fiji and Malaysia (9). In Costa Rica, for instance, there is documentation of a high rate of obesity in older females which is not occurring in males. Mean cholesterol levels are also close to 200 mg/dl (8). In Asia and the Pacific countries, a high prevalence of functional difficulties (chewing, hearing, seeing, walking 300 m) were uncovered but with differential frequency across nations.

Some of the pitfalls associated with the interpretation of studies on ageing and the elderly have been identified (2). It is possible to penetrate to the true intrinsic and extrinsic effects of aging only to avoiding confusion factors of selective survival, cohort effects, and differential environmental challenge. It is felt the comparative multinational and multicultural studies allow for a more profound understanding of the universal aspects of aging and the intrinsic and extrinsic modifiers, since the truly common elements can be extracted from contrasting geographical experiences (9).

Declining mortality in infants and children and higher life expectancy in the last fifty years in developing countries are changing the structure of the population. The percentage of the

elderly in the population has increased and this trend is expected to continue. This increase will lead to social and economic problems due to associated high risk of disability and morbidity and the need for medical services if not properly addressed.

Cognisant of the fact that there are very few studies on the elderly in East Asia, and that nutrition plays a very important role in the well-being and health of the individual, East Asian countries (China, Indonesia, Malaysia, the Philippines and Thailand) and Latin American countries (Brazil, Mexico and Guatemala) decide to undertake a cross-cultural research on nutrition and the elderly. The research project will be carried out in the five East Asian and the three Latin American countries but shall also include collaboration of three European countries, The Netherlands, Germany and Italy, in view of their experience and expertise in the EC concerted action on nutrition and the elderly.

The cross cultural collaboration will permit the East Asian and Latin American countries to characterise the elderly population chronologically as well as biologically, to describe the factors affecting the nutritional status of the elderly, to describe the non-nutritional factors that affect nutrition and health of the elderly; and to compare their findings. The information collected will not only enrich the body of nutrition knowledge but will also serve as important inputs to policies and programmes that can be designed to address the nutritional-health problems of the elderly. Moreover, the cross cultural comparisons may enable the countries to determine the similarities and differences in the parameters used in the study which can serve as database for planning to strengthen research in the field of nutrition particularly concerning the elderly.

General objectives

It is the general objective of the cross-cultural study to identify the nutritional situation of urban and rural elderly in developing countries to generate hypotheses which stimulate and strengthen further research networking between the participating research centres.

Specific objectives

1. to describe and compare the socio-economic background of the elderly according to the
   * region (East Asian, Latin American and Europe),
   * country,
   * rural vs urban setting,
   * income groups, formal education and occupation
   * age (adult aged 35-40 years vs elderly aged 60-70 years),
   * gender.
2. to describe the dietary intake and food habits of the elderly (24-hour recall and food frequency method), and the factors affecting these food habits.
3. to determine and compare the nutritional and health status of the elderly particularly in terms of:
   a. anthromometric measures,
   b. haematologic measures (haemoglobin, haematocrit),
   c. health status, including blood pressure
   d. self- perceived health status and health problems;
4. to characterise and compare non-nutritional variables that effect the food intake, health and nutritional status of the elderly, specifically:
   a. physical activities
   b. social activities

c. use of drugs, tobacco, etc.

d. socio-demographic-economic situation;

5. to elaborate hypotheses and research proposals for future collaborative studies between the participating research centres.

Population to be studied and design

To meet these objectives, the study will be performed in selected rural and urban communities in East Asia and Latin America. The socio-economic-demographic characteristics of the chosen communities should be comparable to that of the national averages of the country for rural and urban communities. Because of possible drop-outs, at the beginning of the study the sample size should be chosen large enough so that at the end of the study data are available of at least a total of 200 rural and 400 urban individuals. The elderly age group of 60 to 70 years should be compared with adults aged 35 to 40 years. Independently living rural and urban individuals should be selected randomly. Urban individuals should have lived at least 5 years in the urban area. All groups are differentiated by gender. Institutionalised urban elderly may be included into the study additionally. However, psycho-geriatric patients in nursing homes and those who are not able to answer the questions independently will not be considered in the study.

Variables

The study is cross-sectional in nature and is made up of two components:

1. **Core** which consists of the block for which data collections is obligatory for all centers:
   a. community profile
   b. socio-demographic-economic characteristics of subjects,
   c. lifestyle: physical activity, social activity, percepcion on health, use of drugs, etc.
   d. dietary intake - food and nutrients
   e. food believes and behavior,
   f. anthropometry - height, weight, skinfold (biceps, triceps, subscapular, suprailiac), circumferences (upper arm, waist and hip), armspan, knee height,
   g. blood values of haemoglobin and haematocrit.
2. **Optional**, comprising the block for which additional data may be collected depending on the resources and capabilities of the cooperating/collaborating institu-

		Urban		Rural	Total
		Low income	Middle income		
60-70 years	Men	50	50	50	150
	Women	50	50	50	150
35-45 years	Men	50	50	50	150
	Women	50	50	50	150
Total		200	200	200	600

tions. This may include on more of the following:

a. blood analyses such as
   * proteins (albumin)
   * blood sugar
   * lipids (cholesterol, HDL),
   * vitamins (such as Vit. A, B vitamins, Vit. D, Vit. E, etc.)
   * minerals (such as ferritin for Fe stores, etc).

b. basal metabolic rate determinations.

Sophisticated and expensive analysis (e.g. for micronutrients) which need appropriated laboratory equipment shall be studied under the responsibility and expertise of the European research centres.

Attempts will be made to assess the biological age of the individuals. The selection of appropriate and representative indicator (s) is subject for further discussions.

To obtain comparable data, methods and procedures will be standardised. The country representatives will meet and agree on the prescribed methodology, after which a manual of operations will be made and intensive training for research personnel will be conducted. The research protocols of the Euronut-EC concerted action on nutrition and health in the elderly and IUNS on nutrition and elderly will be used as guides and their research instruments where applicable may be adopted and used in the study.

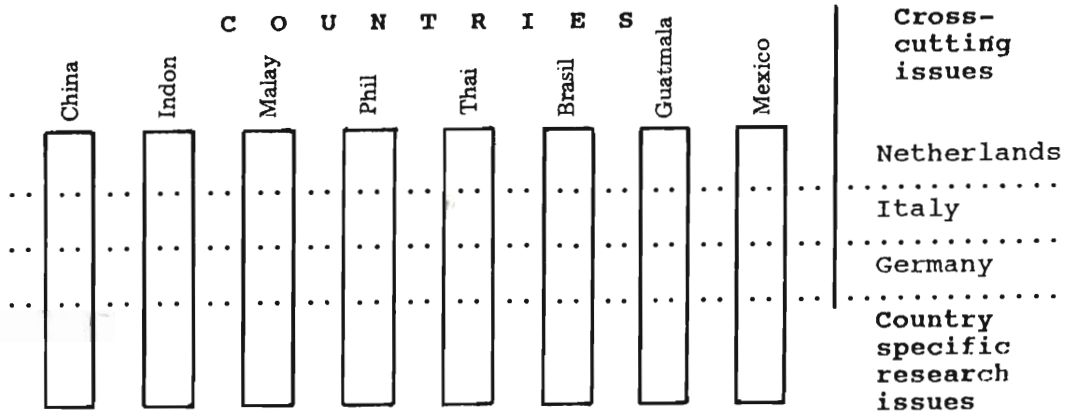
Research sites

Individuals of both, urban and rural communities will be observed in the proposed study. However, for the sake of an acceptable reliability and accuracy the individuals of each study group will be either urban or rural. Following research sites are chosen:

	Urban	Rural
East Asia:		
China	Beijing	x
Indonesia	Jakarta	x
Malaysia	Kuala Lumpur	x
Philippines I	Manila	
Philippines II		x
Thailand	Bangkok	x
Latin America:		
Brazil	Sao Paulo	x
Guatemala	Guatemala C.	x
Mexico	Mexico C.	x

The methodology used in analysis of the specific data shall be formulated as identically as possible to the EC-EURONUT-SENECA study because these methodologies have been tested for applicability and reliability. In addition this allows a comparison of the old European vs. the newly collected data from the developing countries to be drawn. However, the final decision about the detailed methodological procedure shall be made during the first workshop supported by the proposed research project, since the research protocol has to be adapted to the local conditions of each of the study sites. A first draft has been already elaborated during a workshop in Kuala Lumpur in September 1991.

According to the following shown graphic, the centres of the research site will have a vertical responsibility, meanwhile the European centres take over a horizontal responsibility, cross-cutting issues. The data shall be processed and analyzed by each associated proposer of the study site separately, and simultaneously according to the cross-cutting issue by the respective European centre.



References

1. Kinsella KG. Aging in the Third World. CIR Staff Paper #35. Washington, D.C. Centre for International Research, U.S. Bureau of the Census, 1988.
2. Health of the elderly. Report of a WHO Expert Committee. Technical Report Series 779, Geneva, World Health Organizations, 1989.
3. Popkin BM and Bisgrove EZ. Urbanization and nutrition in low-income countries. Presented in ACC/SCN symposium on urbanization and nutrition. Monograph 1987.
4. Lowik MR, Schrijver J, Odink J, van den Berg H, Wedel M, Hermus RJ. Nutrition and aging: nutritional status of "apparently healthy" elderly (Dutch nutrition surveillance system). Journal of American College of Nutrition 1990; 9:18-27.
5. Diet and Health: Implications for Chronic Disease Risk. Washington, D.C. National Academy of Sciences, Press, 1988.
6. Munro HN, Suter PM, Russell RM. Nutritional requirements of the elderly. Annual Review of Nutrition 1987; 7:23-49.
7. Ehrlich K, Litvak J, El envejecimiento y los paisesen desarrollo de la region de las Americas. Bol Ofic Sanit Panamer 1981; 91:312-519.
8. LLanos G (ed.) estudio de la Tecera Edad en Coronado, Costa Rica. Monografias de la OPS/OMS Serie Salud del Adults 1990; 90-01.
9. Andrew GR. Health and ageing in the developing world. In: Evered D. Whelan J (eds.) Research and ageing population. Chichester: Wiley 1980; 17-37.

Proc 6th ACN 1991: 177

Safety issues for natural anticarcinogens in foods

John N Hathcock

Food and Drug Administration, Washington, DC, USA

Abstract

Safety issues for natural anticarcinogens in foods may arise because of the biological activity of these substances. The anticarcinogenesis per se is safe because it is the inhibition of an adverse process. The biological and metabolic mechanism of the anticarcinogenic effect may or may not have undesirable side effects. Much research data indicates that two major mechanisms of anticarcinogenesis are through the antioxidant effect and through enzyme induction. Natural antioxidants in foods include ascorbic acid, tocopherols, carotenes, and a wide variety of nonnutritive antioxidants such as flavonoids, polyphenols and sulfur compounds. Because of the general toxicity of activated oxygen species, the process of antioxidation is frequently beneficial. These benefits include inhibition of the damage caused by activated forms of carcinogens. The side effects which result from excessive intake of antioxidants depend on the chemical identity of the antioxidant, i.e., the nonantioxidative effects of polyphenols are very different from those of sulfur compounds. Inducers of the cytochrome P-450 family of phase I enzymes, have many metabolic efects, including that of enhancing the metabolism of many carcinogens. These activities occur in endoplasmic reticulum of many tissues, but are highly active in the liver. At excessive intakes, many inducers cause pathology of the liver. This increased metabolism usually leads to decreased potency of the carcinogen. The increased activities of the cyctochromes P-450 and conjugating enzymes alter the metabolism of many substances other than carcinogens. For example, barbiturates and phenolic compounds alter the metabolism and increase the requirements for vitamin a and vitamin D. Selection of foods to increase dietary intake of natural anticarcinogens could have adverse effects. More research is needed to establish the optimal levels of natural anticarcinogens.

Proc 6th ACN 1991: 178

Problems of Mycotoxins in foods

CC Ho

Dept. of Genetics & Cellular Biology, University of Malaya, Kuala Lumpur, Malaysia.

Abstract

Mycotoxins produced by various species of *Aspergillus, Penicillium* and *Fusarium* are of public health importance through contamination of foods and animal feed. Their seriousness can be assessed by analysis from reported cases of mild and acute fatal incidents of intoxications. Long term consumption of aflatoxins and fumonisins contaminated foods have been correlated with high incidence of liver and esophagel cancer respectively. A recent case of presumptive acute fatal aflatoxin food poisoning occurred in October 1988 in Perak, Malaysia with deaths of 13 children was associated with consumption of 'loh see fun' (a Chinese noodle) from a common source. Aflatoxins were detected in various organs of these children. Results of experiments carried out to determine the most significant point of high aflatoxin contamination in the sequential process of 'loh see fun' manufacture will be discussed.

Control of mycotoxin intoxications is dependent on proper agricultural practices of cultivation, processing and storage; technology of mycotoxin decontamination by physical, chemical and biological means and stringent legal limits of permitted levels of mycotoxins in human foods and feed.

Proc 6th ACN 1991: 179-181

Effects of enzyme inhibitors and antinutrients in foods

Iwai K, Fushiki T, and Higuchi M

Faculty of Home Economics, Kobe Women's University, Higashisuma and The Department of Food Science and Technology, Faculty of Agriculture, Kyoto University, Japan

The occurrences and properties of a variety of enzyme inhibitors and antinutrients have been reported. However, little information is available on their oral effects on mammals. In this symposium, our recent work on the effects on rats of oral administrations of ovomucoid, known as a trypsin inhibitor in egg white, and of winged bean lectin, as an antinutrient, will be presented.

During the course of our studies on the pancreatic enzyme secretion in rats, we found a new active peptide, designated "monitor peptide", in pancreatic juice. This peptide, which comprises 61 amino acid residues, is trypsin-sensitive and possesses cholecystokinin (CCK) (a polypeptide hormone) releasing activity. The peptide is secreted with proenzymes into the duodenum from the pancreas via the pancreatic duct and is digested by trypsin in the proximal small intestine. During the postabsorptive state, this monitor peptide that is secreted from the pancreas is destroyed though digestion. However, when food protein, which is able to bind with trypsin as substrate, comes into the lumen at a post-prandial phase, the monitor peptide which is a potent secretagogue for CCK, survives the digestive process intact (1), owing presumably to the proteases being too busily engaged in the digestion of food proteins. On the other hand, Gibbs *et al.* in 1973 have reported that intraperitoneal (I.P.) injection of CCK reduced feeding in the intact rat and this suppression of feeding was dose-related for both solid and liquid foods (2). These findings led us to investigate the effects of oral administration of ovomucoid on rat food intake. As shown in Table 1, oral administration of ovomucoid was found to bring about a suppression of food intake, and the suppression was reversed by I.P. administration of a potent CCK antagonist, 0.2 mg of CR 1409 per rat, 1 hour before feeding (Table 2). Also, during the feeding with ovomucoid, the rat plasma CCK levels were extremely elevated to 21.0 $\pm$ 5.4 pg/ml after 30 min, 23.8 $\pm$ 10.7 pg/ml after 1 hour and 30.9 $\pm$ 10.4 pg/ml after 2 hours, while the control rat plasma CCK levels were 6.7 $\pm$ 2.0 pg/ml, 7.6 $\pm$ 3.1 pg/ml and 7.0 $\pm$ 2.2 pg/ml, respectively. The rat plasma CCK levels increased as the concentration of ovomucoid increased in the diet. These results suggest that the ovomucoid in the diet stimulated the secretion of intact monitor peptide in the lumen with the effect of raising the plasma CCK levels and suppression of food intake in the rat.

To investigate the effect of winged bean lectin, a fraction possessing high hemagglutinating activity, but with a negligible degree of trypsin inhibitory activity was isolated from the ripe seeds obtained from Thailand, and orally administered to growing rats in a basal diet containing 10 per cent casein. The food intake and body weights of rats decreased as the level of lectin increased and significant hemagglutinating activity was found in the faeces with an antigenicity identical to that of the native lectin before its feeding. A high incidence of mortality was observed at higher levels of lectin within a short period. A 10 per cent level of lectin in the basal diet caused a significant decrease in the activities of various intestinal enzymes and serious damage to the intestinal mucosa of the rats (3). Experimental results with highly purified winged bean lectin labelled with iodo [2-^{14}C] acetic acid also indicated that the lectin remained intact in the gastrointestinal tract while a part of it was bound to the intestinal mucosa, the rest being excreted directly into faeces (4).

TABLE 1

Effect of coated ovomucoid on rat food intake

	Food intake	
	Ovomucoid# 6.7%	Casein## 6.7% (control)
0.5 hours	2.47 ± 0.93 g	3.42 ± 0.71 g *
1 hour	4.44 ± 1.42	5.86 ± 1.59 *
2 hours	7.05 ± 1.76	8.48 ± 1.80 *

Values were expressed Means ± SD (n = 20)

* Significant difference ($p < 0.05$)

\# Ovomucoid, 6.7 per cent, was mixed with a stock diet (Oriental Co Ltd, Type MF) and administered. Ovomucoid highly purified from egg white was coated with hydrozypropyl methyl cellulose phthalate in a weight ratio of 1 : 4 to avoid the influences of a sensory effect and of a possible digestion by stomach juice

\## For the control diet, 6.7 per cent of casein was mixed with the same stock diet and administered. Casein was also coated as described above and used

TABLE 2

Effect of CCK antagonist* on suppression of food intake by ovomucoid

	Food intake (g)	
	Ovomucoid	Casein (control)
0.5 hour	3.85 ± 1.23	3.53 ± 1.46
1 hour	4.15 ± 1.12	4.33 ± 2.19
2 hours	5.20 ± 0.76	5.50 ± 1.57
3 hours	7.26 ± 1.17	8.01 ± 1.44
4 hours	10.73 ± 2.46	11.89 ± 1.88

Values were Mean ± SD (n = 10).

* CR 1407 (from Rotta Co.), as a CCK antagonist was given via I.P., 0.2 mg per rat, 1 hour before feeding.

References

1. Iwai K, Fushiki T, Fukuoka S-I. Pancreatic enzyme secretion mediated by novel peptide: Monitor peptide hypothesis. Pancreas 1988; 3: 720-8.
2. Gibbs J, Young RC, Smith GP. Cholecystokinin elicits satiety in rats with open gastric fistulas. Nature 1973; 245: 323-5.
3. Higuchi M, Tsuchiya I, Iwai K. Growth inhibition and small intestinal lesions in rats after feeding with isolated winged bean lectin. Agric Biol Chem 1984; 48: 695-701.
4. Higuchi M, Kawada T, Iwai K. In vivo binding of the winged bean basic lectin labelled with iodo [2-^{12}C] acetic acid to the intestinal epithelial cells of the rat. J Nutr 1989; 119: 490-5

Proc 6th ACN 1991: 182-188

Drug metabolism and toxicity in malnutrition

Kamala Krishnaswamy

Food and Drug Toxicology Research Centre, National Institute of Nutrition, Jamai Osmania, Hyderabad - 500 007, India

Introduction

Human diets are a complex mixture of chemicals and essential nutrients. Both the nutrients and non-nutrients have the potential to alter metabolism and disposition of xenobiotics (1, 2). The xenobiotics in turn can significantly alter the nutritional status. Thus the nutrient drug interactions can result in altered therapeutic response in terms of efficacy and toxicity of drugs, chemically-induced diseases and nutritional stress. The duration and intensity of drug action depend on several factors such as absorption, protein binding, bio-transformation by the liver and other tissues and clearance by the kidney. The very basis of pharmacological action depends upon the concentration of drugs and its metabolites in the region of the receptor and their interactions. Over the past two decades, considerable effort has been directed towards the study of drug metabolism, and *in vivo* clearance of drugs in the malnourished. (3). This review includes some of the recent issues concerned with drug therapy in malnourished human host in developing countries.

Pathophysiology and drug metabolism

Several pathophysiological changes occur in protein-energy malnutrition and in major vitamin/mineral deficiency disorders (1, 3, 4). A series of physiological, pathological, functional and biochemical changes are encountered in several tissues. Therefore, one can contemplate changes in absorption in response to a variety of physiological changes in the alimentary tract; binding, distribution and tissue concentrations of drugs as a sequalae to alterations in the body proteins and composition; in hepatic and renal clearance of drugs due to altered structural and functional changes in the liver and kidney and ultimately the pharmacodynamic profile due to changes in the intermediary metabolism, endocrine alterations and immunological functions. The important drug nutrient interactions can be considered from five angles. (a) The effects of food on absorption of drugs and drug absorption *per se* in malnutrition. (b) Competitive binding to proteins and its pharmacokinetic and clinical significance. (c) Alterations in bio-transformation - metabolic rates and clearance of drugs by both liver and kidney. (d) Therapeutic efficacy and toxicity of drugs, and (e) Drug-induced nutritional deficiencies. The above arises as a result of physical, physiological, bio-chemical and pharmacological interactions between dietary components and xenobiotics.

Absorption

A drug given by enteral route, through processes such as disintegration, dissolution, absorption and passage through the liver, reaches the systemic circulation. Both the quantity and quality of foods have been shown to enhance or decrease the bioavailability of a number of drugs such as antihypertensives, antibiotics, anti-inflammatory compounds and anti-convulsants (5, 6). Several mechanisms have been implicated in such food-drug interactions. Absorption of drugs in malnutrition is yet another facet of the problem. Studies on anti-tuberculous drugs, anti-malarials, antibiotics and nutrients used as medicaments have shown that malnutrition delays and decreases absorption of such important medicaments which can result in therapeutic failures (6, 7). Further observations suggest that the absorption of poorly available substances (as determined by its *in vitro* characters) are much more impaired in malnutrition as compared to better available substances. Thus the bio-pharmaceutic characters of the drugs add to impaired absorption in malnutrition resulting in therapeutic failures (8, 9).

Drug protein binding distribution

The plasma is a complex solution containing different proteins of which albumin and L_1 acid glycoprotein are important as they transport endogenous and exogenous substances. The binding determines not only the availability of free drug but also the tissue distribution of drugs. Malnutrition reduces the binding of acidic drugs to albumin (10) though its effect on basic drugs binding to L_1 acid glycoprotein is in the opposite direction (11). In addition to the distribution, plasma protein binding can also alter the pharmacokinetic parameters depending upon the metabolic characteristics of the drug. As the intensity of pharmacological effect is a function of the free drug in plasma, it may be surmised that in malnutrition, there will be an increase in the maximum intensity of the pharmacological effect while the duration of effect may increase or decrease depending on the dose and the minimum effective free drug levels and the time course of the free drug concentration. Even though clinical information is scanty, it is obvious that the low clearance drugs, where binding is the limiting factor for clearance, the metabolism is directly proportional to the free drug concentration and therefore several of the drugs tend to get either eliminated faster or slower depending upon the severity of malnourished state and its direct effects on bio-transformations.

Bio-transformation of drugs

The foreign compounds that enter the body are either excreted unchanged by the liver or the kidney or they undergo enzymatic reactions leading to inactivation. Several groups of enzymes participate in the bio-transformation of drugs and endogenous substances. Estimates of relative safety, potential efficacy and extent of action can be predicted from the quantitative studies on bio-transformation and the clearance of drugs from the body.

Adequate nutrition is an important factor for proper handling of xenobiotics. Experimental evidences suggest that nutrients are required for metabolism of foreign compounds. (12, 13). As it is difficult to extrapolate the experimental results to clinical situations, studies have been designed to investigate the effect of nutritional factors in malnourished adults and children.

Effect of protein-energy malnutrition on oxidative metabolism of drugs

The bio-transformation of drugs

depend on the membrane bound Cyt P 450 mediated monooxygenases, the flavoprotein NADPH Cyt P 450 reductase and phosphatidyl choline which are an expression of genetic and environmental factors. The environmental factors may be physical, chemical or physiological in nature which either induce or inhibit the enzymes. A large number of nutrients are involved in the functioning of these enzymes (12,15). Clearance of prototype drugs such as antipyrine has been studied in several grades of malnutrition. In adults, it has been observed that in mild and moderate forms of malnutrition, the oxidative metabolism of drugs is in an induced state (16). The total body clearance of drugs such an antipyrine (16), phenylbutazone (17), rifampicin (18), doxycycline (19) in undernourished appear to be much higher as compared to normal subjects. On the other hand, the clearance of antipyrine is significantly reduced in severe states of malnutrition as encountered in cases of famine oedema (16).

Our recent findings on phynytoin metabolism, suggest that the rate of metabolism as determined by KM and V-max varies depending upon the severity of the malnourished state (unpublished). It is evident that in individuals with albumin below 3g/dl, due to hepatic involvement V-mas is lower as compared to mild and moderately malnourished individuals with serum albumin levels between 3-4 g/dl, who in fact have a high clearance as compared to normals with albumin levels of 4-4.5 g/dl. Drug oxidation in malnourished children with drugs such as antipyrine (20,21), theophylline (22,23), and phenobarbitone (24), yielded interesting results both before and after rehabilitation. In severe protein-energy malnutrition, namely kwashiorkor and marasmus, a decrease in the enzyme levels and a reduced elimination of drugs from the body, which after rehabilitation improves and reaches near normal values have been documented. Caution needs to be exercised for drugs with narrow margin of safety and dose-dependant kinetics with severe toxic reactions.

Effect of malnutrition on conjugation

Conjugations appear to be a versatile system of reactions which regulate the elimination of toxic substances which include drugs and their metabolites and carcinogens. Though conflicting reports exist on conjugations, the general consensus appears to be that they are compromised in different grades of malnutrition. In addition to enzymes *in vivo* co-factor availability is also compromised. Chloramphenicol, paracetamol and sulphadiazine conjugations along with the D-glucuronic acid excretions confirm that conjugations and clearance of drugs are impaired with accumulation in protein-energy malnutrition. (4,25). The enzyme studies in adults indirectly lend support to these observations with paranitrophenol conjugation being lower in individuals with low body mass index and serum albumin levels (26).

Macronutrient effects on drug metabolism

Studies on drug clearance in free-living populations are always difficult as several factors at different levels complicate the results.

Metabolic studies on healthy subjects under controlled conditions can provide better information. Such studies on antipyrine, theophylline, (27,28), caffeine (29) suggest higher clearance of drugs when the energy percentage from proteins is in the order of 40-50% as compared to 10-12% of protein energy in the diet. Fagan *et al.* (30) recently reported that high protein diet (40 energy %) can increase metabolism of even high clearance

drugs such as propranalol. Krishnaswamy *et al.* (31) have evaluated antipyrine and aminopyrine kinetics on varying protein and carbohydrate intakes. The results suggest that drug oxidations are impaired when the calorie intakes are 1.2 X BMR whereas at intakes of 1800 calories they remain unaltered. Protein energy percentage when increased from 10-20% can stimulate the drug metabolism even on low calorie intakes while in subjects on low proteins, carbohydrates even if adequate does not maintain drug clearances in the normal. The non-nutrient components in the diet seem to be as important as the nutrients (32, 33). Drug diet interactions therefore are quite complex and difficult to predict.

Renal clearance

Urinary excretion is the primary route of elimination of water-soluble compounds. Renal functional reserve is related to protein intake (34). Further diet-induced change in pH and ionisation will also alter re-absorption of drugs. Aminoglycosides such as gentamicyn and streptomycin need extra care in severely malnourished children and adults (4).

Toxicity in malnutrition

One of the major concerns of modern therapy is adverse drug reactions. Several factors can contribute to the development of drug toxicity. Available evidence on animal experiment support the view that malnutrition increases drug toxicity (35). The human studies on pharmacokinetics reinforce the findings and suggest that the malnourished are predisposed to more toxic reactions.

Two of the recent studies on hepatotoxic reactions to drugs in India demonstrate a higher hepatotoxic reaction to a combination of rifampicin and INH both in children (36) and adults (37). Anthracycline-induced cardiomyopathy was much higher in the malnourished (38). Behavioural abnormalities were high in malnourished children treated with phenaborbitone (24). Hypoalbuminemics tend to be more susceptible to drug toxicity (39). As essential nutrients and non-nutrients co-exist in the diets, it is also important to consider the chemically-induced diseases such as cancer in relation to diet. The recent research efforts in this direction indicate that metabolic susceptibility to carcinogens is much higher in the malnourished subjects (40, 41, 42) with micronutrient deficiencies further increasing the risk of cancers.

Drug-induced nutrient deficiencies

Drugs can interact with specific constituents of diet, particularly nutrients in several ways. Among the drug-nutrient interactions, those that induce significant nutritional deficiencies as adverse reactions need to be considered particularly in malnourished population. A number of mechanisms are involved by which drugs induce nutrient deficiencies, which include effects on intake, absorption, transport, metabolism, and excretion of nutrients. (44,45). The drug-nutrient interactions can often go unrecognised as many of them may be sub-clinical and rarely manifest. Our understanding on drug-induced disorders of bone and mineral metabolism are still rudimentary. Rifampicin a potent inducer of microsomal systems and isonicotinic acid on inhibitor of mixed function oxidase are often administered as first and second line of therapy in tuberculosis. Rifampicin, a potent enzyme inducer, has recently been shown to reduce 25 (OH)D by 70%, accompanied by increased oxidation of antipyrine and elevated beta-hydroxy cortisol (46). INH when used along with rifampicin has been demonstrated to result in a decrease in antipyrine clearance, fall in serum calcium and phosphate,

25(OH)D and elevated parathyroid hormone concentration (47). Our studies on calcium phosphorous levels along with bone densitometric studies in both wellnourished and undernourished patients of tuberculosis receiving INH and rifampicin clearly demonstrate that the adverse effects of these drugs are more in the undernourished. It is further suggested that the osteopenia can be prevented by a good diet (48).

Conclusion

It is evident that specific dietary components, nutritional status and environmental factors can interact and influence drug pharmacokinetics and dynamics in malnutrition. Such interactions in general can result in decreased therapeutic efficacy and increased susceptibility to toxic reactions. Food-drug interactions in the gastrointestinal tract can alter the availability and the plasma drug concentrations. The nutritional effects on hepatic bio-transformations appear to have more impact in children with severe grades of malnutrition as compared to adults and mild and moderate forms of malnutrition. Metabolic toxicity including chemical carcinogenesis and drug-induced nutrient deficiencies are likely to be higher. Further studies are required on the prevalence of toxic reactions to drugs in the malnourished, as a variety of drugs are in use in clinical practice.

References

1. Krishnaswamy K. Effects of malnutrition on drug metabolism and toxicity in humans. In: Hathcock JN, ed. Nutritional Toxicology. New York: Academic Press Inc 1987: 105-123.
2. Hathcock JN. Metabolic mechanisms of drug nutrient interactions. Fed Proc 1985; 44: 124-129.
3. Krishnaswamy K. Drug metabolism and pharmacokinetics in malnutrition. Trends Pharmacol Sci 1983; 4: 295-299.
4. Krishnaswamy K. Drug metabolism and pharmacokinetics in malnourished children. Clin Pharmacokinet 1989; 17: 66-88.
5. Melander A, McLean A. Influence of food intake on pre-systemic clearance of drugs. Clin Pharmacokinet 1983; 8: 286-296.
6. Krishnaswamy K. Effect of food on drug bioavailability. In: Sharma KN, Sharma KK, and Sen P, eds. Proceedings of the Indo-US symposium/workshop on genetic drugs, bioequivalence and pharmacokinetics, 1988; 187-192.
7. Raghuram TC, Krishnaswamy K. Tetracycline absorption in malnutrition. Drug Nutr Interact 1981; 1: 23-29.
8. Santosh KK, Raghuram TC, and Krishnaswamy K. Bioavailability of different brands of tetracycline in undernourished subjects. Brit J Clin Pharmacol (Communicated).
9. Reddy V, Srikantia SG. Serum vitamin A in kwashiorkor. Am J Clin Nutr 1966; 18: 105-109.
10. Buchanan N. Drug protein binding and protein energy malnutrition. S Afr Med J 1977; 52: 733-737.
11. Jagadeesan V, Krishnaswamy K. Drug binding in undernourished: A study on the binding of propranolol to acid glycoproteins. Eur J Clin Pharmacol 1985; 27: 657-659.
12. Campbell TC. Nutrition and drug metabolising enzymes. Clin Pharmacol and Ther 1977; 22: 699-706.
13. Basu TK. Nutritional status and drug therapy. In: Clinical implications of drug therapy. Florida: CRC Press, 1980; 2: 61-95.
14. Conney AH. Induction of microsome cytochrome P 450 enzymes. Life Sci 1986; 39: 2493-2518.

15. Krishnaswamy K. Nutrients/Non-nutrients and drug metabolism. Drug Nutrient Interact 1985; 4: 235-245.

16. Krishnaswamy K, Naidu NA. Microsomal enzymes in malnutrition as determined by plasma half life of antipyrine. Br Med J Clin Res 1977; 1: 538-540.

17. Krishnaswamy K, Ushasri V, and Naidu NA. The effect of malnutrition on the pharmacokinetics of phynylbutazone. Clin Pharmacokinet 1981; 6: 152-159.

18. Polasa K, Murthy KJR, and Krishnaswamy K. Rifampicin kinetics in undernutrition. Br J Clin Pharmacol 1984; 17: 481-484.

19. Raghuram TC, Krishnaswamy K. Pharmacokinetics and plasma steady levels of doxycycline in undernutrition. Brit J Clin Pharmacol 1982; 14: 785-789.

20. Narang RK, Mehta S, and Mathur VS. Pharmacokinetics study of antipyrine in malnourished children. Am J Clin Nutr 1979; 20: 1979-1982.

21. Buchanan N. Effect of protein energy malnutrition on drug metabolism. Wld Rev of Nutr & Dietet 1984; 43: 129-139.

22. Eriksson M, Paalzow L, Bolme P, *et al.* Pharmacokinetics of theophylline in Ethiopian children of differing nutritional status. Eur J Clin Pharmacol 1983; 24: 89-92.

23. Feldman C, Hurchinson VE, Pipenger CE, *et al.* Effect of dietary protein and carbohydrate on theophylline metabolism in children. Pediatr 1980; 66: 956-962.

24. Singh LM, Mehta S, Wohra RM, *et al.* Monitoring of phenobarbitone in epileptic children. Int J Clin Pharmcol, Ther & Toxicol 1987; 25: 18-22.

25. Mehta S, Kalsi HK, Jayaraman S, *et al.* Chloramphenicol metabolism in children with protein calorie malnutrition. Am J Clin Nutr 1975; 28: 977-981.

26. Ramesh RP, Kalamegham R, Chary AK, *et al.* Hepatic drug metabolising enzymes in undernourished men. Toxicol 1985; 37: 259-266.

27. Anderson KE, Conney AH, Kappas A. Nutrition and oxidative drug metabolism in man: relative influence of dietary lipids carbohydrate and protein. Clin Pharmacol Ther 1979; 26: 493-501.

28. Anderson KE. Influences of diet and nutrition on clinical pharmacokinetics. Clin Pharmacokinet 1988; 14: 325-346.

29. Juan D, Worwag EM, Schoeller DA, *et al.* Effects of dietary protein on theophylline pharmacokinetic and caffeine and aminopyrine breath tests. Clin Pharmacol Ther 1986; 40: 187-194.

30. Fagan TC, Walle T, Oexmann MJ, *et al.* Increased clearance of propranalol and theophylline by high protein compared with high carbohydrate diet. Clin Pharmacol Ther 1987; 41: 402-406.

31. Krishnaswamy K, Kalamegham R, and Naidu NA. Dietary influences on the kinetics of antipyrine and aminopyrine in human subjects. Br J Clin Pharmacol 1984; 17: 139-146.

32. Conney AH, Pantuck EJ, Hsiao KC, *et al.* Regulations of human drug metabolism by dietary factors. Ciba Foundation symposium 1980; 76: 147-167.

33. Monks TJ, Caldwell J, Smith RL. Influence of methylxanthian containing foods on theophylline metabolism and kinetics. Clin Pharmacol Ther 1979; 26(4): 513-524.

34. Park GD, Spector R, Kitt TM. Effect of dietary protein on renal tubular clearance of drugs in humans. Clin Pharmacokinet 1989; 17: 441-451.

35. McLean AEM, Witts DJ, Tame D. The influence of nutrition and inducers on mechanisms of toxicity in humans and animals. Ciba Foundation Symposium 1980; 76: 275-288.

36. Rugmini PS, Mehta S. Hepatotoxicity of isoniazid and rifampicin in children. Ind Paediatr 1984; 21: 119-126.

37. Krishnaswamy K, Prasad CE, Murthy KJR. Hepatic dysfunction in undernourished patients receiving isoniazid and rifampicin. Ttop Geogr Med (Communicated).

38. Obama M, Cangir A, Van Eys J. Nutritional status and anthracycline cardiotoxicity in children. South Med J 1983; 76: 577-578.

39. Boston Collaborative Drug Surveillance Program. Diphenylhydantoin side effects and serum albumin level. Clin Pharmacol Ther 1973; 14: 529-532.

40. Doll R, Peto R. The causes of cancer, quantitative estimates of avoidable risks of cancer in US today. J Natl Can Inst 1981; 66: 1203-1233.

41. Ramesh RP, Krishnaswamy K. Difference in response of glucuronide and glutathione conjugation enzymes of aflatoxin B_1 and N-Acetylaminofluorene in underfed rats. J Toxicol Environ Hlth 1988; 103-109.

42. Jagadeesan V, Krishnaswamy K. Effect of food restriction on benzo(a)pyrene DNA binding in wistar rats. Toxicol 1989; 56: 223-226.

43. Krishnaswamy K. Malnutrition and chemical carcinogenesis. Proceedings of Vth Asian Congress of Nutrition 1987, pp 392-295.

44. Roe DE. Risk factors in drug induced nutritional deficiency. In: Roe DA, and Campbell TC, eds. Drugs and Nutrients. New York: Marcel Dekker, 1984: 503-523.

45. US Department of Health and Human Services. The Surgeon General Report on Nutrition and Health. Publication No. 88-50210. 1988, pp 671-684.

46. Brodie MJ, Boobis AR, Hillyard CJ, *et al.* Effect of isoniazid on vitamin D metabolism and hepatic monooxygenase activity. Clin Pharmaco Ther 1980; 30: 363-367.

47. Brodie MJ, Boobis AR, Hillyard CJ, *et al.* Effect of rifampicin and isoniazid on vitamin D metabolism. Clin Pharmacol Ther 1982; 32: 525-530.

48. Krishnaswamy K. The interactive effects of protein energy malnutrition and drugs with special emphasis on minerals and bone. In: Proc XIV Int Congress Nutr Seoul 1989: 351-354.

Proc 6th ACN 1991: 189-202

The value of perioperative nutritional support

Micheal M Meguid, Maureen Galvin

Department of Surgery, University Hospital, SUNY Health Service Science Centre at Syracuse, Syracuse, New York 13210, USA

Introduction

Almost 50 years ago, Studley (1) showed that a preoperative weight loss of more than 20% in patients undergoing surgery for benign chronic peptic ulcer was associated with a mortality of 33.3% compared with 3.5% in those with a lesser weight loss. This observation has been followed by others relating nutrient deficits or malnutrition and impaired host metabolic and immunological defence mechanisms. Despite numerous studies showing the link between deficient preoperative nutritional status and poor operative outcome, there appears to be no uniform acceptance that the use of perioperative nutritional support for either the malnourished patient or the patient at high risk of developing malnutrition is of benefit in decreased incidence of postoperative complications.

We will specifically examine: (a) the impairment in the malnourished patient; (b) the methods now used to identify malnourished patients preoperatively; (c) those prospective studies which are limited to evaluating the use of perioperative (pre- or postoperative) nutritional support in patients already committed to operative intervention; (d) indications for nutritional support that are based on the primary diagnosis(es) and include **all potential** candidates for surgery, regardless of their nutritional status at time of hospitalisation; and finally (e) the disadvantages of perioperative nutritional support.

Physiological impairments in the malnourished patient

Patients with a preoperative weight loss of more than 20% had a postoperative morality of 33.3% vs. 3.5% in those with lesser weight loss (1). By the mid 1930's and early 1940's, hypoproteinaemia was documented as leading to delayed gastric emptying and prolonged ileus (2), increased incidence of wound dehiscence (3), delayed bone callus formation (4), and increased risk of infection (5). Subsequently, these early observations were extended to show that postoperative complications were more frequent in hypoproteinaemia surgical patients (6), and that malnourished burned children had an increased risk of developing sepsis (7). Thus, in a variety of different subjects and with different insults, similar results were obtained, leading to the common conclusion that complications are more likely to occur in the poorly nourished state. More recent studies have once more demonstrated this association in a variety of clinical settings (8-12).

The mechanisms by which malnourished patients are more prone

to postoperative infections are often synergistic in producing their deleterious effects. Mechanical breakdown of the skin and mucosal barriers by surgical incisions and manipulations lead to contamination by microorganisms and is unavoidable. Consequently, a normal host defence mechanism is essential to pre-functions incude reduced cell-mediated immunity and inflamatory response (13) with decreases in humoral or antibody components (B-lymphocytes), cell-mediated components (T-lymphocytes), phagocytic components (polymorphonuclear neutrophils, macrophages, reticuloendothelial system) and complement (direct or alternate pathway)(14, 15). The consequence of this impaired immunological state is an increased postoperative complication rate.

Malnutrition also affects skeletal muscle function. A reduction of muscle bulk and muscle metabolism occurs; this is the most recognisable aspect of gross malnutrition. Impairment of the respiratory muscles leads to reduction of both the vital capacity and the resting minute ventilation (16); moderate starvation alone has been shown to cause a significantly impaired hypoxic ventilatory response (17). Cardiac mass and contratility are reduced (18). Renal function may be impaired from a fall in glomerular filtration rate secondary to the malnutrition-related decrease in circulatory volume (19). Fibroplasia is also reduced in malnourished patients with resultant delayed wound healing (20). Starvation decreases brain neurotransmitters, leading to a state of apathy with diminished sense of self motivation (21). Thus, since malnutrition has a deleterious effect on virtually every major system in the body, it is not surprising that increases in morbidity and mortality occur following operative trauma in malnourished patients.

Identification of the malnourished patient

Many anthropometric, biochemical and immunological tests and body composition analyses were developed to nutritionally assess a patient. However, no single nutritional index can fully characterise the extent of malnutrition. Therefore, several investigators have used a few simple tests in a stepwise regression analysis or in a discriminant analysis in order to increase the sensitivity and specificity of the diagnosis of malnutrition (9,10,22,23,24). Mullen *et al.* (22) and Buzby *et al.* (9) developed a prognostic nutritional index (PNI) to evaluate patient prior to operations for gastrointestinal cancer. The PNI was based on serum albumin level, triceps skinfold thickness, serum transferrin level, and delayed cutaneous hypersensitivity reactivity to three recall antigens. Using this index, three risk groups of patients were identified: low (PNI < 40%), intermediate (PNI = 40%-49%) and high (PNI > 50%). The incidence of all postoperative complications was 8% for the low, 30% for the intermediate, and 46% for the high risk groups. Mortality rates were 3%, 4.3%, and 33%, respectively. In a subsequent study of perioperative TPN, the same authors reported a reduction in postoperative complications, major sepsis and mortality in patients at high risk by the PNI criteria (23); the absence of intermediate effects suggsts that the inappropriately narrow PNI range of intermediate risk is notably not valid.

Harvey *et al.* (24) formulated a hospital prognostic index using the diagnosis, serum albumin level, delayed cutaneous hypersensitivity reactivity, and the presence of sepsis. Ryan and Taft (25) studied serum albumin and transferrin levels, lymphocyte count and delayed cutaneous hypersensitivity reactivity. No significant relationships were noted between changes in the measured indices and the incidence of postopera-

tive complications.

A carefully performed history and physical examination has been proposed as the best available nutritional assessment tool (26,27). Called `subjective global assessment', it was tested preoperatively in 59 general surgical patients. Nutritional status was assessed by the standard nutritinal assessment techniques and was compared to the `global assessment' performed by two physicians with a nutritional educational background. There was a significant association between the severity of malnutrition as judged by the physicians and that assessed by the nutrition assessment techniques. Furthermore, the `subjective global assessment' was related to outcome (infection) in the mild and severe malnourished patients with a 78% sensitivity and 70% specificity. However, another group of investigators (28) using similar techniqus, were able to confirm these results.

Prospective studies

We have identified 22 prospective studies on perioperative nutritional support in English from 1977 to 1991: nine papers on preoperative TPN vs Oral; two papers regarding preoperative TPN vs TEN, four papers on postoperative TPN vs Oral; two studies on postoperative TEN vs Oral; and five studies on postoperative TPN vs TEN. Not only were a wide variation in the amount of calories and nitrogen given, but also the amounts given were not clearly stated in some reports. Hence, we have to assume for the purpose of this review that each investigator fulfilled the cardinal condition of nutritional support, namely, to meet each patient's energy and nutrient requirements.

Preoperative TPN

Holter and Fischer (29) studied 56 patients with preoperative malnutrition who had comparable operations for gastrointestinal cancer. They found that the use of TPN prior to surgery in malnourished patients reduced the postoperative complication rate from 19.2% to 13.3%, but this difference was not statistically significant. A group of control patients who had not lost weight had only a complication rate of 7.1% after operation, this difference also was not significant. Mortality was 0% in the well-nourished patients, 6.6% in the group receiving TPN, and 7.6% in the malnourished patients not receiving TPN. This study, although generally well designed, suffered from the Type II statistical error. Moghisis *et al.* (30) demonstrated that preoperative TPN resulted in positive nitrogen balance, while patients receiving only an oral diet and intravenous fluids (without amino acids) remained in negative nitrogen balance and had inferior wound healing. Heatley *et al.* (31) compared a high protein oral ward diet (n=36) to a treatment group receiving the same oral diet plus TPN (n=38) for 7-10 days preoperatively. There were no significant differences between the two groups when comparing preoperative weight loss, immunologic status or serum albumin levels. Total complication rate was 35.4% in the study group and 83% in the control group (ns). Wound infection rate in the group receiving preoperative TPN was significantly less ($p<0.05$) at 7.7% compared to 30.5% in the control group. However, the incidence of anastomotic leakage was similar in both groups, as was a fairly high mortality rate. The authors reported that catheter complications (occlusion, infection or thrombosis) were common but not generally serious. The authors concluded that it was doubtful whether the small reduction in wound infection observed and the costs and risks of the procedure, justified the routine use of preoperative TPN in patients whose nutritional status was impaired by gastrointestinal malignancy.

Bellantone *et al.* (32) prospectively

randomised well nourished and malnourished patients with a variety of gastrointestinal diseases prior to resective operation to receive either a standard hospital diet or preoperative TPN for at least 7 days. The incidence of postoperative sepsis was similar in both control an study groups. However, when only malnourished patients were considered, those who received preoperative TPN had a lower incidence of postoperative sepsis (21% vs 53.5%, $p<0.05$) compared to their counterparts who did not receive TPN. In the subgroup of malnourished patients with gastric neoplasia, septic complications occurred in 100% of the patients in the control group and in only 16.7% in the study group ($p<0.05$). Postoperative mortality (<5%) was similar in both groups.

In a prospective study evaluating 125 patients with gastrointestinal carcinoma, Mueller *et al.* (33) randomised patients to receive either a regular hospital diet or preoperative TPN for 10 days. The diet contained 2400 kcal/day. Sixty percent of all the patients were considered malnourished on admission (weight loss > 5kg in the last 3 months, serum albumin <3.5 g/dl and negative response to five skin tests), and the incidence of malnutrition was similar in both groups after randomisation. While patients in the study group gained approximately 2 kg, the controls lost about 1 kg weight on average. Serum albumin was restored in the group receiving TPN, but decreased in the controls. The incidence of major complications (defined as intraabdominal abscess, peritonitis, anastomotic leakage and ileus) was significantly reduced in the TPN group (19% vs 11%, respectively, $p<0.05$). The cause of pneumonia in the control group was not stated, but more patients required ventilatory support compared with the TPN group ($p<0.05$). Operative mortality was 11% and 3%, respectively ($p<0.05$). The patients in the control group who developed postoperative complications were given TPN.

Using study admission criteria based on the prognostic nutritional index (PNI) of Mullen *et al.* (22), Smith and Hartemink (34) randomised 34 patients who had a PNI greater than 30% to preoperative TPN or oral diet. After randomisation, the two groups were well matched for age, sex, and nutritional status. Major complications occurred in 35.3% of the control group and in 17.6% of the study group; the mortality rates were 17.6% and 5.9% respectively. However, neither difference was statistically significant, probably because of the insufficient number of cases.

Meguid *et al.* (35) designed a prospective trial to study approximately 160 malnourished patients with solid tumors of the gastrointestinal tract. Patients were assigned to receive either preoperative TPN or a hospital diet, followed postoperatively by TPN in both groups to determine whether preoperative TPN alone in only malnourished patients resulted in improved postoperative clinical outcome. To determine the endpoint of biologically effective preoperative nutritional repletion, restoration to normal of abnormal muscle function was used. Muscle function was evaluated by electricly stimulating the ulnar nerve to the adductor pollicis muscle at 10,20 and 50 Hz with between 90 and 120 V, as previously described (36). F10/F20 and relaxation rate (percentage force loss/10 ms at 20 Hz) were measured on admission and then every other day in response to nutrient intake, until muscle-function tests were stable.

The postoperative study endpoint was taken as the end of the inadequate oral nutrient intake period (IONIP)(37), when the patients were eating 60% of their preoperative estimated caloric requirements, at which point TPN was stopped. This figure was taken because

it represents restoration of gastrointestinal tract function sufficient to allow the patient to consume enough nutrients to meet resting energy requirements, and a stage of convalescence after which readmission for nutritional problems would not occur. Postoperative complications (defined as all complications requiring therapeutic intervention), death, and length of postoperative hospital stay were documented.

During the first 2 years of study, 3 malnourished cancer patients were randomised to the control and 32 patients to the study groups. Of the 34 control patients, 19 had complications after operation; there were no deaths. Patients were started on an oral diet after the operation, and by day 12 (range 7-30 d) ate 60% of their estimated caloric requirements. They were discharged a median of 14 days (range 9-30 d) after the operation.

After admission, the 32 study patients received TPN (average intake 40±3 kcal/kg and 0.3±0.2g N/kg/d). The endpoint of the preoperative TPN in the study group, defined as improvement on a previously abnormal muscle-function test, was reached at a median of 9 days. After the operation, 10 patients had a complication, and one death occurred. After the operation, patients were started on an oral diet, as deemed appropriate by their attending surgeon, and reached their endpoint of 60% of estimated caloric intake on day 8 (range 7-30+ d). Patients were discharged a median of 10 days (2-30 d) after the operation.

The study admission F10/F20 of 0.56±0.04 (M±SE) was within the normal range, but relaxation rate (8.9±0.7) was consistent with that observed in subclinical postoperative malnutrition. With the delivery of nutrients by TPN, F10/F20 remained unchanged, but a significant ($9<0.05$) improvement occurred in relaxation rate, to 11.3±1.5 during the 9 day preoperative TPN period. This improvement is consistent with decreased muscle fatiguability and an improvement in stamina (38).

The study was terminated prematurely by the principal investigator for a couple of reasons. The first was the repeated expressed bias of referring surgeons to have their patients participate in the study only if they were to be randomly assigned to receive TPN, underscoring the difficulty in performing such studies. The other reason was the observation by the principal investigator that in patients ramdonised to receive TPN, numerous "fine-tuning" of physiological systems, primarily pulmonary and cardiac, occurred by the primary surgeon during the preoperative TPN period in order to optimize the patient's condition before the upcoming operation, thereby introducing subtle factors that could affect clinical outcome but that were not relevant to nutritional repletion.

Fan *et al.* (39) examined the efficacy of 2 weeks of preoperative TPN for the prevention of complications after operation for esophageal cancer in 40 patients. There were no significant differences in age, nutritional status, tumor staging, or histology between the two groups of patients. The use of preoperative parenteral nutrition resulted in a significant gain in body weight but failed to produce an overall reduction in postoperative morbidity and mortality rates. However, patients receiving preoperative parenteral nutrition exhibited two types of changes in serum albumin concentrations. Those with a fall in serum albumin concentrations associated with an increase in body weight had a significantly higher incidence of postoperative pulmonary complications than the group exhibiting a rise in serum albumin concentrations concomitant with an increase in body weight. On the basis of their data, the authors concluded that 2

weeks of TPN might not be adequate in certain patients and a longer period of 2 weeks of TPN was required; there was no clinical benefit from the routine use of preoperative TPN in all patients; and TPN may benefit a select group of patients. However, this group was not identified.

More recently, the results of the long-awaited multicentre Veterans Affairs TPN study was published (40). Three hundren ninety-five malnourished patients requiring laparotomy or non-cardiac thoracotomy were randomly assigned to one of two groups. The study group received TPN for 7-15 days before the operation and 3 days afterward. The control group received cystalloids and an oral diet, as indicated, for >3 days before the operation and for the first 72 hours after the operation. Thereafter, TPN or tube feeding could be instituted, if clinically indicated. The patients were monitored for complications for 90 days thereafter. The rates of major complications during the first 30 days after surgery in the two groups were similar. An increased rate of infection vs complications occurred in patients categorized as either borderline or mildly malnourished, in whom TPN had no demonstrable benefit. In contrast, severely malnourished patients who received TPN had fewer noninfectious complications than did control subjects (5% vs 43% ; p=0.03), with no concomitant increase in infectious complications. The data showed that the use of preoperative TPN in patients who are severely malnourished helped to reduce complications. It was further concluded that the use of preoperative TPN should be limited to patients who are severely malnourished unless there are other specific indications.

From the above studies on preoperative TPN, it seems that significant improvements in the patient's nutritional status occurs when TPN is given to severely malnourished patients in adequate amounts for >7-15 days. In most studies, fewer complications occurred in those patients receiving TPN. This was most clearly shown in study of Mueller *et al.* (33) and to a certain degree in the Veterans Affairs TPN Cooperative study (40). In other studies (22,32,40), preoperative TPN decreased the incidence of complications after operative procedures in only the most malnourished patients. It is unlikely that TPN given for < 7 days in the preoperative period will be effective in reducing postoperative complications. Finally, these studies once more emphasise that the key issue may be suitable identification of the high-risk patient.

Preoperative TPN vs TEN

Lim *et al.* (41) randomised 24 patients with total dysphagia from carcinoma of the esophagus to receive either TPN (12 patients) or TEN via a gastrostomy tube (12 patients) for a minimum for 3 weeks before operation. The lower morbidity and mortality obseerved in the TPN group did not reach statistical significance, in part probably because of the small numbers. Sako *et al.* (42) prospectively randomised 69 patients in a comparison of TPN vs TEN for preparing patients with head and neck cancer for operation. Nutritional support was given for at least 14 days. Nitrogen balance was significantly better in the TPN group. Both groups had lower complications rates vs historical controls, but no differences were found with regard to postoperative complications and mortality between the TPN or TEN groups.

These two studies suggest that when given in adequate amounts in the preoperative period, there is no difference between the enteral or parenteral route of nutrient administration as regards postoperative incidences of complications and death; although nutritionally supported patients had

fewer complications than historic controls.

Postoperative TPN vs Oral Intake

Collins *et al.* (43) compared intravenous amino acids alone in one group vs oral intake in a second (control) group and TPN in a third (study) group, each of 10 patients having either abdominaloperineal resection of the rectum or panproctocolectomy. Weight loss before operation ranged from 0-30% and was equally distributed among the groups. TPN resulted in a shorter period for perineal wound healing and a decrease in the incidence of postoperative sepsis, both significantly ($p<0.50$) different from controland peripheral intravenous amino acids. Thus, the infusion of crystalline amino acids alone was not effective as TPN.

Preshaw *et al.* (44) evaluted whether 6 days of TPN would reduce the incidence of colonic fistula after colonic anastomosis. The serum albumin was above 3.5 g/dl in both control and study groups. TPN infusion was started 24 hours before operation and continued until 5 days after operation. NO changes occurred in the nutrition indices evaluated before and after the operation in both groups. The incidence of radiologically detected anastomotic leaks were: 17% in oral group and 33% in TPN group (ns). The authors stopped the study when 21 pairs of patients had entered because they considered it unethical to continue a trial which would eventually show that TPN is worse than standard postoperative therapy.

Yamada *et al.* (45) compared postoperative TPN and oral intake in patients subjected to non-curative gastrectomy for advanced gastric cancer and then given chemotherapy. The survival rate for non-curative resection and the disease-free interval were both greater in the group receive TPN. In this study, TPN enabled the therapeutic dose of chemotherapy to be given, thereby explaining the prolonged disease-free interval.

Woolfson and Smith (46) investigated the possibility that morbidity and mortality might be reduced by giving 7 days of elective TPN starting immediately after major thoracoabdominal procedures or after total cystectomy. With a standard postoperative fluid regimen, TPN had no effect on morbidity, mortality, or duration of hospital stay in a group of 122 sequentially recruited patients. Although the authors thought that there may be certain patients who might benefit from postoperative TPN, they were unable to identify them with simple preoperative assessment. The authors recognised that to test the efficacy of a new or different therapeutic regimen such as TPN, > 1000 patients would be needed in each treatment arm to be 90% sure of not missing a difference in beneficial effect, if one was present, at a type I significance level of 5%.

The studies of Collins *et al.* (43) and Yamada *et al.* (45) suggest that the use of TPN in the postoperative period significantly reduces complications and deaths after major abdominal operations as compared to oral intake. In contrast, Preshaw *et al.* (44) and Woolfson and Smith (46) were unable to demonstrate any benefit of the use of TPN. Preshaw *et al.* evaluated only well-nourished patients in whom the rationale for giving TPN is questionable, whereas Woolfson and Smith studied patients whose nutritional status was ambiguous.

Postoperative TEN vs Oral Intake

Although gastic dysfunction usually prevents early oral or gastric feeding after abdominal operations, the small bowel regains its motility soon after operation, allowing its use for TEN as an alternative to TPN. Study groups received immediate enteral feeding,

while control groups were fed only after the apparent resumption of gastrointestinal function.

In the study by Sagar *et al.* (47), Flexical R (Mead Johnson Nutritionals, Evansville, IN) was used in the postoperative period and led to a reduction in weight loss, length of hospital stay and an improvement in nitrogen balance, as compared to controls. Moore and Jones (48) evaluated the use of Vivonex HN (Norwich Eaton Pharmaceuticals, Norwich, NY) started immediately after operation. An enhanced nitrogen balance and an increased albumin level occurred with the group receiving TEN. However, in both studies, the immediate postoperative daily caloric intakes were greater in the TEN groups, hence the comparison was really or nutritional support versus none rather than a true comparison of route.

Both studies above have demonstrated improved surgical outcome in the groups receiving TEN in the postoperative period as compared to controls.

Postoperative TPN vs TEN

Since both TPN and TEN have each been shown to effectively reduce nitrogen loss and provide a greater nitrogen and caloric intake as compard to an ad lib oral diet, the question arises as to which is more effective postoperatively. Thus, a series of prospective randomised studies compared TPN vs TEN after abdominal operations (49-53). Despite some metabolic differences encountered with the use of TEN or TPN in some of these studies (50, 52), the overall results indicated that they yield similar rates of morbidity, mortality and duration of hospital stay when used postoperatively, whether the patients underwent gastrointestinal or pancreticobiliary procedures or laparotomy for trauma.

Thus, when enteral and parenteral nutrition were prospectively compared in patients who could receive either, there was no apparent advantage of one route of nutritional support over the other, and both seemed to be effective in improving operative outcome.

Use of perioperative nutritional support based on primary diagnosis

If one were to accept that perioperative nutrition would be of benefit for reducing postoperative complications only in the malnourished patients, one would falsely conclude that well-nourished patients are rarely, if ever, candidates for perioperative nutritional support. In certain clinical situations, the indication for perioperative nutritional support may be based on the primary diagnosis regardless of patient's nutritional status at the time. General examples include the firm expectationof a prolonged inadequate oral nutrient intake period following operation (embodying the concept of IONIP [54]), or situations in which the patient develops an acute clinical condition with concomitant nutritional gastrointestinal tract, since such patients are often potential candidates for one or more operations because of the unpredictable clinical course of the primary diagnosis.

A specific example as to whether the primary diagnosis should affect the decision to start perioperative nutritional support on admission irrespective of nutritional status is severe acute biliary pancreatitis, usually occurring in a previously otherwise healthy and well-nourished patient. This disorder frequently warrants long periods of bowel rest and one or maybe more operations. The early institution of TPN in these patients may prevent the severe nutritional depletion that often follows severe protracted pancreatitis, as well documented by Blackburn *et al.* (55). Even though TPN may have no particular effect upon the acute disease process in the pancreas, TPN may serve

two useful purposes in the treatment of acute pancreatitis: (a) maintaining the nutritional status of patients with protracted gastrointestinal tract dysfunction secondary to pancreatitis and its co-morbidities, and (b) correcting pre-existing nutritional abnormalities (56, 57). Since gastrointestinal dysfunction may be further aggravated by the necessity of repeated laparotomies, TPN should thus be started once the diagnosis is established, or at the latest, after the first laparotomy. The reported evidence indicates that prompt and vigorous use of TPN may be crucial to the survival of these severely ill patients, particularly if operative intervention is likely to be subsequently needed.

Another specific example is the enterocutaneous fistula. These patients are at high risk of developing early malnutrition and often require multiple ancillary surgical procedures to assist fistula closure. The incidence of malnutrition among patients with enterocutaneous fistulas varies from 20% to 74% (58), and from 20% to 70% of these patients will require an operation to close the fistula (59, 60). Because the eventual need for operation is often unpredictable, nutritional support is indicated in anticipation of prolonged functional starvation due to long period without a normally functioning gastrointestinal tract. There is also evidence that nutritional support may promote spontaneous' closure of enterocutaneous fistulas in 20-80% of the cases, thus avoiding operation altogether (59-68).

A third specific example for perioperative nutritional support based on diagnosis alone is in inflammatory bowel disease, particularly Crohn's disease. In a prospectiv randomised study it was shown that 35% to 47% of the patients required surgical procedures (69). More recently, in a trial including 67 patients admitted with complications of Crohn's disease, operation was necessary in 25% (70). Acute complications of inflammatory bowel disease are thus conditions in which operative intervention may be needed; the benefits from TPN include bowel rest, maintenance of nutritional status, or even replenishment of the nutritionally depleted patient. Two groups have evaluated the use of preoperative TPN in the treatment of Crohn's disease. In a retrospective study including 30 patients with Crohn's disease, those who received preoperative TPN for at least 5 days had significantly fewer postoperative complications than those who did not; all complications that occurred were in those patients who have severe protein depletion (71). Forty-four patients with severe active Crohn's disease and abdominal masses, fistula and/or obstruction, received preoperative TPN for a mean period of 33 days (70). The authors noted significant improvements in body weight, plasma albumin and total proteins, and remissions in the active inflammatory process. No death occurred; the major complication rate was only 6%. Although the beneficial effects of preoperative TPN reported in these retrospective studies have not been confirmed in prospective randomised studies, they suggest strongly that perioperative nutritional support may be an important adjunct to the surgical treatment of inflammatory bowel disease.

Disadvantages of the use of perioperative nutritional support

The database upon which the surgeon will make his decision as to whether or not perioperative nutritional support is indicated must also consider the potential disadvantages of the methods. These fall into two major groups: safety of perioperative nutritional support, and cost.

A detailed discussion of the complications associated with TPN or enteral

nutrition is beyond the scope of this review. However, perioperative nutritional support is indicated on an elective basis for patients who will be submitted to a well-planned operation and therefore, the risks of mechanic, septic or metabolic complications associated with TPN in such patients are probably low. The arguement for the use of perioperative nutritional support on an elective basis is reinforced by studies reported above in which few complications directly related to the nutritional support occurred. In the meta-analysis reported by Detsky *et al.* (72), the risk of developing an iatrogenic complication secondary to TPN intervention was 6.7%; although most of these are minor complications.

The second potential disadvantage of the use of perioperative nutritional support is the cost involved; this requires consideration of the cost-effectiveness of this treatment. The direct costs of TPN include those of catheter insertion, roentgenograms, intravenous solutions, hepaarin, laboratory tests and hospital stay. The additional costs exclusively related to TPN in hospitalised patients were reported to range from $75 to $503 per day (73, 74). The cost-effectiveness of preoperative TPN has been estimated to reduce (74) or to increase (75, 76) the total hospitalisation cost per patient. The cost-effectiveness ratio will obviously improve when the attributed benefit of TPN in risk reduction of a certain disease state improves. According to Detsky *et al.* (75), the costs of TPN are substantially higher if a low estimate for risk reduction (i.e., 20%) is used. Therefore, these calculations stress the need for careful patient selection in order to improve the cost-effectiveness of perioperative nutritional support.

Summary and conclusions

Analysis of the studies described above suggest that 2-3 days of preoperative TPN does not improve outcome, while TPN for 5-7 days may influence outcome, and more than 7 days of preoperative TPN is associataed with significant improvement in reduction of postoperative morbidity and mortality; provided that adequate amounts of nutrients are given to patients at high risk. When a functioning gastrointestinal tract permits, preoperative TEN appears to be as effective as TPN in nutritional replenishment. The use of postoperative nutritional support by either TEN or TPN yields reduction of postoperative complications as compared to postoperative ad lib oral nutrition. Finally, it is proposed that (a) there exists a group of patients at high risk for complications and death from their disease, regardless of their nutritional status, (b) that they can be identified on admission even though they are only potential, not all actual, candidates for operations, and (c) in these patients the prompt initiation of enteral or parenteral nutrition may notably reduce hospital morbidity, length of stay, and mortality. Research needs to focus on two primary areas: (i) Development of refined criteria for patient selection; and (ii) Development of specific and sensitive criteria for the determination of nutritional depletion and, more important, for nutritional repletion.

References

1. Studley HO. Percentage of weight loss: A basic indicator of surgical risk in patients with chronic peptic ulcer. JAMA 1936; 106:458-460.
2. McCray PM, Barden RP, Ravdin IS. Nutritional edema, its effect on gastric emptying time before and after gastric operations. Surgery 1937; 1:53-64.
3. Thompson WD, Ravdin IS, Rhoads JE, Frank IL. Use of lyophil plasma in correction of hypoproteinaemia and prevention of wound disruption. Arch Surg 1938; 36:509-518.

4. Rhoads JE, Kasinskas W. Influence of hypoproteinaemia on formation of callus in experimental fracture. Surgery 1942; 11:38-44.
5. Cannon PR, Wissler RW, Woolridge RL, *et al.* The relationship of protein deficiency to surgical infection. Ann Surg 1944; 120:514-525.
6. Rhoads JE, Alexander CE. Nutritional problems of surgical patients. Ann NY Acad Sci 1955; 63:268-275.
7. Neumann CG, Lawlor GL, Stiehm ER, *et al.* Immunologic responses in malnourished children. Am J Clin Nutr 1975; 28:89-104.
8. Seltzer MH, Bastidas JA, Cooper DM, Engler P, Slocum B, Fletcher SH. Instant nutritional assessment. JPEN 1979; 3:157-159.
9. Buzby GP, Mullen JP, Matthews DC, Hobbs CL, Rosato EF. Prognostic nutritional index in gastrointestinal surgery. Am J Clin Nutr 1980; 139:160-167.
10. Kaminski MV, Fitzgerald MJ, Murphy RJ, *et al.* Correlation of mortality with serum transferrin and anergy. JPEN 1977; 1:278 (Abs).
11. Thomas R. Relationship of albumin to mortality in critically ill respiratory patients. Am J Clin Nutr 1979; 32:246-254.
12. Reinhardt GF, Myoofski JW, Wilkens DB, *et al.* Incidence and mortality of hypoalbuminemic patients and hospitalised veterans. JPEN 1980; 4:357-360.
13. Meakins JL, Christou NV, Shizgal HM, MacLean LD. Therapeutic approaches to anergy in surgical patients. Ann Surg 1979; 190:286-296.
14. Christou NV. Anergy testing in surgical patients. Infect Surg 1983; 10:692-700.
15. Kahan BD. Nutrition and host defence mechanism. Surg Clin N Amer 1981; 61:557-570.
16. Askanazi J, Weissman C, Rosenbaum SH, *et al.* Nutrition and the respiratory system. Crit Care Med 1982; 10:163-172.
17. Doekel RC Jr, Zwillich CW, Scoggin CH, *et al.* Clinical semi-starvation: depression of hypoxic ventilatory responses. N Engl J Med 1976; 295:358-361.
18. Kyger ER 3rd, Block WJ, Roach G, Dudrick SJ. Adverse effects of protein malnutrition on myocardial function. Surgery 1978; 84:147-156.
19. Klahr S, Allenye GA. Effects of chronic protein-calorie malnutrition on the kidney. Kidney Int 1973; 3:129-141.
20. Bozzetti F, Terno G, Longoni C. Parenteral hyperalimentation and would healing. Surg Gynecol Obstet 1975; 141:712-714.
21. Wurtman RJ, Hefti F, Melamed E. Precursor control of neurotransmitter synthesis. Pharm Rev 1980; 32:315-335.
22. Mullen JL, Buzby GP, Waldman MT, Gertner MH, Hobbs CL, Rosato EF. Prediction of opertive morbidity and mortality by preoperative nutritional assessment. Surg Forum 1979; 30:80-82.
23. Mullen JL, Buzby GP, Matthews DC, Smale BF, Rosato EF. Reduction of operative morbidity and mortality by combined preoperative and postoperative nutritional support. Ann Surg 1980; 192:604-613.
24. Harvey KB, Moldawer LL, Bistrian BR, Blackburn GL. Biological measures for the formulation of a hospital prognostic index. Am J Clin Nutr 1981; 34:2013-2022.
25. Ryan JA, Taft DA. Preoperative nutritional assessment does not

predict morbidity and mortality in abdominal operations. Surg Forum 1980; 31:96-98.

26. Baker JP, Detsky AS, Wesson DE, *et al.* Nutritional assessment: A comparison of clinical judgement and objective measurements. N Engl J Med 1982; 306:969-972.
27. Detsky AS, Baker JP, Mendelson RA, Wolman SL, Wesson DE, Jeejeebhoy. Evaluation of accuracy of nutritional assessment techniques applied to hospitalised patients: Methodology and comparisons. JPEN 1984; 8:153-159.
28. Pettigrew RA, Charlesworth PM, Farmilo RW, Hill GL. Assessment of nutritional depletion and immune competence: a comparison of clinical examination and objective measurements. JPEN 1984; 8:21-24.
29. Holter AR, Fischer JE. The effects of perioperative hyperalimentation on complications in patients with carcinoma and weight loss. J Surg Res 1977; 23:31-34.
30. Moghissi K, Hornshaw J, Teasdale PR, Dawes EA. Parenteral nutrition in carcinoma of the esophagus treated by surgery: nitrogen balance and clinical studies. Br J Surg 1977; 64:125-128.
31. Heatley RV, Williams RHP, Lewis MH. Preoperative intravenous feeding: A controlled trial. Postgrad Med J 1979; 55:541-545.
32. Bellantone R, Doglietto GB, Bossola M. *et al.* Preoperative parenteral nutrition in the high risk surgical patient. JPEN 1988; 12:195-197.
33. Mueller JM, Dienst C, Brenner U, Pichlmaier H. Preoperative parenteral feeding in patients with gastrointestinal carcinoma. Lancet 1982; 1:68-71.
34. Smith RC, Hartemink R. Improvement of nutritional measures during preoperative parenteral nutrition in patients selected by the prognostic nutritional index: A randomised controlled trial. JPEN 1988; 12:587-591.
35. Meguid MM, Curtas MS, Meguid V, Campos AC. Effects of preoperative TPN on surgical risk - preliminary status report. Br J Clin Prac 1988; 42:53-58.
36. Jeejeebhoy DN, Meguid MM. Assessment of the nutritional status in the oncologic patient. Surg Clin N Ajm 1987; 66:1077-1090.
37. Meguid MM, Campos ACL, Meguid V, Debonis D, Terz JJ. IONIP: A criterion of surgical outcome and patient selection for perioperative nutritional support. Br J Clin Prac 1988; 42:8-14.
38. Meguid MM, Curtas S, Chen M, Nole E. Adductor pollicis muscle tests to detect and correct subclinical malnutrition in preoperative cancer patients. Am J Clin Nutr 1987; 45:843 (Abst).
39. Fan ST, Lau WY, Wong KK, Chan YPM. Preoperative parenteral nutrition in patients with oesophageal cancer: a prospective, randomised clinical trial. Clin Nutr 1989; 8:23-27.
40. Veterans Affairs Total Parenteral Nutrition Cooperative Study Group. Perioperative total parenteral nutrition in surgical patients. N Engl J Med 1991; 325:525-532.
41. Lim STK, Choa RG, Lam KM, *et al.* Total parenteral nutrition versus gastrostomy in the preoperative preparation of patients with carcinoma of the esophagus. Br J Surg 1981; 16:391-402.
42. Sako K, Lore JM, Kaufman S, Razack MS, Bakamjian V, Reese P.

Parenteral hyperalimentation in surgical patients with head and neck cancer: A randomised study. J Surg Oncol 1981; 16:391-402.

43. Collins JP, Oxby CB, Hill GL. Intravenous amino acids and intravenous hyperalimentation as protein-sparing therapy after major surgery. A controlled clinical trial. Lancet 1978; 1:788-791.
44. Preshaw RM, Attisha RP, Holligsworth WJ, Todd JD. Randomised sequential trial of parenteral nutrition in healing of colonic anastomoses in man. Can J Surg 1979; 22:437-439.
45. Yamada N, Koyama H, Hioki K, Yamada T, Yamamoto M. Effect of postoperative total parenteral nutrition (TPN) as an adjunct to gastrectomy for advanced gastric carcinoma. Br J Surg 1983; 70:267-274.
46. Woolfson AMJ, Smith JAR. Elective nutritional support after major surgery: a prospective randomised trial. Clin Nutr 1989; 8:15-21.
47. Sagar S, Harland P, Shields R. Early postoperative feeding with elemental diet. Br Med J 1979; 1:293-295.
48. Moore EE, Jones TN. Nutritional assessment and preliminary report on earlly support of the trauma patient. J Am Coll Nutr 1983; 2:45-54.
49. Yeung CK, Smith RD, Hill GL. Effect of an elemental diet on body composition. Comparison with intravenous nutrition. Gastroenterology 1979; 77:652-657.
50. Muggia-Sullam M, Bower RH, Murphy RF, Joffe SN, Fischer JE. Postoperative enteral versus parenteral nutritional support in gastrointestinal surgery. A matched prospective study. Am J Surg 1985; 149:106-112.
51. Bower RH, Talamini MA, Sax HC, Hamilton F, Fischer JE. Postoperative enteral nutrition: A randomised controlled trial. Arch Surg 1986; 121:1040-1045.
52. Adams S, Dellinger EP, Wertz MJ, Oreskovich MR, Simonowitz D. Johansen K. Enteral versus parenteral nutritional support following laparotomy for trauma: A randomised prospective trial. J Trauma 1986; 26:882-891.
53. Heylen AM, Lybeer MB, Pennickx FM, Kerremans RP, Frost PG. Parenteral versus needle jejunostomy nutrition after total gastrectomy. Clin Nutr 1987; 6:131-136.
54. Meguid MM, Mughal MM, Debonis D, Meguid V, Terz JJ. Influence of nutritional status on the resumption of adequate food intake in patients recovering from colorectal cancer operations. Surg Clin N Amer 1986; 66:1167-1176.
55. Blackburn GL, Williams LF, Bistrian BR, *et al.* New approaches to management of severe acute pancreatitis. Am J Surg 1976; 131:114-124.
56. Goodgame JT, Fischer JE. Parenteral nutrition in the treatment of actue pancreatitis: Effect on complications and mortality. Ann Surg 1977; 186:651-658.
57. Grant JP, James S, Grabowski V, Trexler KM. Total parenteral nutrition in pancreatice disease. Ann Surg 1984; 200:627-631.
58. Edmunds LH Jr, Williams GM, Welch CE. External fistulas arising from the gastro-intestinal tract. Ann Surg 1960; 152:445-471.
59. Kaminski VM, Deitel M. Nutritional support in the management of external fistulas of the alimentary tract. Br J Surg 1975; 62:100-103.
60. McIntyre PB, Rithie JK, Hawley PR, Bartram LL, Lennard-Jones JE. Management of enterocutaneous

fistulas: A review of 132 cases. Br J Surg 1984; 71:293-296.

61. Voitk AJ, Echave V, Brown RA, McArdle AH, Gurd FN. Elemental diet in the treatment of fistulas of the alimentary tract. Surg Gynecol Obstet 1973; 137:68-72.
62. MacFadyen BV Jr, Dudrick SJ, Ruberg RL. Management of gastrointestinal fistulas with parenteral hyperalimentation. Surgery 1973; 74:100-105.
63. Rocchio MA, Mo Che CJ, Haas KF, Randall HT. Use of chemically defined diets in the management of patients with high output gastrointestinal cutaneous fistulas. Am J Surg 1974; 127:148-158.
64. Reber HA, Roberts C, Way LW, Dunphy JE. Management of external gastrointestinal fistulas. Ann Surg 1978; 188:460-467.
65. Soeters PB, Ebeid AM, Fischer JE. Review of 404 patients with gastrointestinal fistula. Impact of parentarel nutrition. Ann Surg 1979; 190:189-202.
66. Thomas RJS. The response of patients with fistulas of the gastrointestinal tract to parenteral nutrition. Surg Gynecol Obstet 1981; 153:77-80.
67. Sitges-Serra A, Jaurrieta E, Sitges-Creus A. Management of postoperative enterocutaneous fistulas: the roles of parenteral nutrition and surgery. Br J Surg 1982; 69:147-150.
68. Rose D, Yarborough MF, Canizaro PL, Lowry SF. One hundred and fourteen fistulas of the gastrointestinal tract treated with total parenteral nutrition. Surg Gynecol Obstet 1986; 163:345-350.
69. Dickinson RJ, Ashton MG, Axon ATR, Smith RC, Yeung CK, Hill GL. Controlled trial of intravenous hyperalimentation and total bowel rest as an adjunct to the routine therapy of acute colitis. Gastroenterology 1980; 79:1199-1204.
70. Gouma DJ, von Meyenfeldt MF, Rouflart M, Soeters PB. Preoperative total parental nutrition (TPN) in severe Crohn's disease. Surgery 1988; 103:648-652.
71. Rombeau JL, Barot LR, Williamson CE, Mullen JL. Preoperative total parenteral nutrition and surgical outcome in patients with inflammatory bowel disease. Am J Surg 1982; 143:139-143.
72. Detsky AS, Baker JP, O'Rourke K, Goel V. Perioperative parenteral nutrition: a meta analysis. Ann Int Med 1987; 107:195-203.
73. Anderson GF, Steinberg EP. DRGs and specialised nutrition support: prospective payment and nutritional support: the need for reform. JPEN 1986; 10:3-8.
74. Twomey PL, Patching SC. Cost-effectiveness of nutritional support. JPEN 1985; 9:3-10.
75. Detsky AS, Jeejeebhoy KN. Cost-effectiveness of preoperative parenteral nutrition in patients undergoing major gastrointestinal surgery. JPEN 1984; 8:632-637.
76. Koretz RL. Preoperative total parenteral nutrition (TPN) in upper gastrointestinal cancer (UGIC): how much for much? Gastroenterology 1983; 84:1214 (Abs).

Proc 6th ACN 1991: 203-205

Dietary calories and fibre in cancer

David Kritchevsky

The Wistar Institute, 3601 Spruce Street, Philadelphia, PA 19104-4268, USA

The role of dietary fibre in cancer remains unresolved. Ecological data would tend to support the original hypothesis of a protective role (1) but reviews of the overall epidemiologic data provide no unanimity as an even more recent review (2) points out. The original hypothesis did not take into consideration the varied nature of dietary fibre nor of its many metabolic effects. Furthermore, in human subjects fibre intake reflects the intake of fibre-rich foods which contain a variety of other components which may also influence carcinogenesis. The possible effects of dietary fibre in the human colon are summarized in Table 1.

Dilution of colonic contents could result in dilution of carcinogens or co-carcinogens and reduction of the possibility of their interaction at the cellular surface. Short chain fatty acids, especially butyric, can suppress cell proliferation. Effects on amount and type of colonic bacteria can influence bile acid and ammonia metabolism which can, in turn, affect carcinogenesis.

Fibre enhances faecal energy loss (3). Thus, in effect, it reduces available calories. Caloric restriction has been studied since 1909 and has been shown to inhibit spontaneous, transplanted or induced tumours in mice and rats. The earliest studies (4) led to an interest in this modality which

TABLE 1

Effects of dietary fibre in the human colon

Increases faecal weight
Increases frequency of defaecation
Decreases transit time
Dilutes colonic contents
Increases microbial growth
Alters energy metabolism
Adsorbs organic and inorganic substances
Decreases dehydroxylation of bile acids
Produces H_2, CH_4, CO_2 and short chain fatty acids

lasted for about a decade and then waned until Tannenbaum's studies in the 1940's which revived interest (5). But that interest, too, lasted for only ten years. Since 1982 we have been working in this area and interest is again renewed. With every return to this area of study we know more about causes and mechanisms of carcinogenesis so that we learn more about the mechanisms underlying the effects of caloric restriction.

In 1943 Lavik and Baumann (6) studied caloric restriction in mice treated with methylcholanthrene to induce skin tumours. When the diet was low in both fat and calories no tumours were observed. A diet high in calories but low in fat led to 93% more tumours than one low in calories but high in fat. Calories played the principal role.

In our early experiments we tested the effects of 40% caloric restriction on growth of DMBA-induced mammary tumours in female Sprague-Dawley rats and DMH-induced colon tumours in male F344 rats. The calorie-restricted diets were designed to provide the same levels of protein, fibre, vitamins, and minerals as did the control diets. The restricted diets contained 2.15 times as much fat, however. Still the total fat contents of the diets were modest. At 40% caloric restriction in diets containing corn oil mammary tumorigenesis was reduced by 75% and colon carcinogenesis by 47%. When the dietary fat was mostly coconut oil, the reductions were even greater. Still, 40% caloric restriction is drastic so the next study was aimed at determining effects of stepwise decrease in calories - by 10, 20 and 30%. The diets were still low in fat (5%). Ten percent caloric restriction did not reduce mammary tumour incidence but reduced tumour multiplicity and tumour burden by 43 and 47%, respectively. At 20% restriction tumour incidence was reduced by 33% but tumour multiplicity and burden were only 7 and 13% lower than on 10% restriction. At 30% restriction, tumour incidence was 42% below that of the controls but tumour multiplicity was 72% lower and tumour burden 91% lower. It was clear that the major effect occurred between 20 and 30% caloric restriction. The next experiment was conducted to determine if caloric restriction exerted its effects in the face of a high fat diet. Three control groups of rats were fed 5, 15 or 20% corn oil and two groups were subjected to 25% caloric restriction and fed 20 or 26.7% corn oil. Thus, they ingest the same amount of fat daily as did rats fed 15 or 20% corn oil ad libitum. In the control groups increasing levels of dietary fat led to increasing mammary tumour incidence, multiplicity and burden. In rats fed 26.7% corn oil and calorically restricted by 25% tumour incidence (compared to rats fed 20% fat ad libitum) was reduced by 63%, tumour multiplicity by 88% and tumour burden by 81%. Clearly, caloric restriction was effective even in the face of a high fat diet.

We have also shown, as have others, that caloric restriction instituted at any stage of the experiment has a positive effect.

What is the mechanisms? In our studies we found that plasma insulin levels were significantly reduced in rats subjected to energy (calorie) restriction. The reduction is observed within one week of institution of the restricted regimen and is maintained throughout the duration of the studies. Levels of plasma IGF-I are reduced for a few weeks then revert to normal and levels of plasma IGF-II are unaffected. Experiments to test the role of insulin are in progress.

How does this relate to human carcinoma? In a study conducted in Canada (7) it was found that risk of colon cancer in men was almost doubled in going from diets containing

TABLE 2

Caloric restriction in carcinogenesis

1. Human epidemiological studies show increasing relative risk of colon cancer with increasing caloric intake.
2. In rats caloric restriction by as little as 10% has beneficial effects.
3. In rats caloric restriction by 25% or more leads to significant reductions in tumour incidence, tumour multi plicity and tumour weight.
4. The caloric restriction effect is independent of level of fat in the diet.
5. Caloric restriction reduces plasma insulin levels which may be one of the mechanisms by which it works.

less than 2485 kcal/day to diets containing more than 3255 kcal/day. In women, going from below 1760 kcal/day to above 2360 kcal/day increased relative risk by a factor of 2.2. A British study (8) found relative risk in men going from 1.0 to 2.3 as caloric intake changed from below 1936 kcal/day to above 2486 kcal/day. A recent American study (9) has similarly striking findings in both men and women and concludes: "Total energy intake must be evaluated before attempting to assign a causal role to any food or nutrient that may be postulated to play a role in colon cancer."

Conclusions are summarized in Table 2. Several reviews of the effects of caloric restriction on carcinogenesis have been published (10-12).

References

1. Committee on Diet, Nutrition and Cancer. (1982) Diet, Nutrition and Cancer, Washington DC.: National Academy Press.
2. Byers T. Cancer 1988; 62: 1713-1724.
3. Southgate DAT, Durnin JVGA. Br J Nutr 1970; 24: 517-535.
4. Moreschi C. Z Immunitatsforsch 1909; 2: 651-675.
5. Tannenbaum A. In: Homburger F, Fishman WH, eds. The Pathophysiology of Cancer. New York: P.B. Hoeber, Inc. 1953; 392-437.
6. Lavik PS, Baumann AC. Cancer Res 1943; 3: 749-756.
7. Jain M, Cook GM, Davis FG, Grace MG, Howe GR, Miller AB. Int J Cancer 1988; 26: 757-768.
8. Bristol JB, Emmett PM, Heaton KW, Williamson RCN. Br Med J 1985; 291: 1467-1470.
9. Lyon JL, Mahoney AW, West DW, Gardner JW, Smith KR, Sorenson AW, Stanish W. J Nat Cancer Inst 1987; 78: 853-861.
10. Kritchevsky D, Klurfeld DM. Am J Clin Nutr 1987; 45: 236-242.
11. Kritchevsky D. Proc Soc Exp Biol Med 1990; 193:35-38.
12. Seindruch R, Albanes D. Kritchevsky D. Hematology/ Oncology Clinics of North America 1991; 5: 79-89.

Proc 6th ACN 1991: 206-212

Dietary fat as a promoter of mammary cancer: evidence pro and con

Kenneth K Carroll

Human Nutrition Centre, Department of Biochemistry, University of Western Ontario, London, Ontario N6A 5C1, Canada

Introduction

In 1982, the Committee on Diet, Nutrition, and Cancer of the U.S. National Research Council concluded "that of all the dietary components it studied, the combined epidemiological and experimental evidence is most suggestive for a casual relationship between fat intake and the occurrence of cancer" (1). More recently, the importance of dietary fat in breast cancer has been questioned, mainly because of the variable results obtained in cohort and case-control studies. The aim of this brief review is to present evidence for and against the hypothesis that dietary fat acts as a promoter of mammary cancer and thus increases the risk of breast cancer in humans.

Experimental and epidemiological evidence

Beginning with the work of Tannenbaum (2), many experimental studies over the past fifty years have shown that mice and rats fed high-fat diets develop mammary tumours more readily than those fed low-fat diets (3-7). This effect of dietary fat appears to be exerted mainly at the promotional stage of carcinogenesis, since mammary tumour yields can be enhanced by feeding a high-fat diet only after exposure to a carcinogen (4) and since the effect has been observed for mammary tumours induced by a variety of carcinogens as well as for spontaneous mammary tumours (8).

These experimental observations, together with epidemiological evidence of a strong positive correlation between dietary fat and breast cancer incidence and mortality in human populations (4,8-10) have stimulated much interest in the role of dietary fat in breast cancer (1,11) and have led to an exponential increase in the number of publications on the subject (12).

Observations on migrants from Europe and Asia to the United States and Australia (13,14), and on time-trend studies within a country such as Japan (15,16) have indicated that the correlation between dietary fat and breast cancer is related to environmental rather than genetic factors. Both types of studies have shown that breast cancer incidence increases with increasing intake of dietary fat.

In contrast to these intercountry, migrant and time-trend studies, prospective cohort studies have provided only weak or in some cases negative evidence of an association between dietary fat and breast cancer (1,11). One of the most influential

cohort studies is that of Willett *et al.* (17) who used questionnaires to follow the dietary intake of nearly 90,000 nurses in the United States over a six-year period. They found that, if anything, there was a negative correlation between breast cancer and estimated dietary fat intake. Another cohort study of more than 5,000 women who participated in the National Health and Nutrition Examination Survey I (NHANES I) likewise showed a significant negative association between dietary fat and risk of breast cancer in a ten-year follow up (18). In a study involving a twenty-year follow up of approximately 4,000 subjects chosen from a larger cohort involved in a dietary survey, Knecht *et al.* (19) reported a non-significant negative correlation between dietary fat and the risk of breast cancer, which became positive when adjusted for energy intake. Howe *et al.* (20) also reported a trend toward increased risk with increasing levels of dietary fat in a sample selected from a cohort of more than 55,000 women involved in a breast screening intervention trial.

Early case-control studies, like the cohort studies, failed to provide strong evidence of an association between dietary fat and risk of breast cancer (11). A number of additional case-control studies have been reported within the past few years from Argentina (21), Australia (22), Canada (23), China (24), Denmark (25), France (26), Greece (27), Italy (28), The Netherlands (29), Russia (30), Singapore (31) and the United States (32). Some of these have shown a positive association between dietary fat and risk of breast cancer (21,23-26,28,29) while others have not (22, 27, 30-32). In a combined analysis of twelve studies, Howe *et al.* (33) found a consistent, statistically positive correlation associated with dietary saturated fat and breast cancer in postmenopausal women.

Intervention studies represent another and more promising approach to studying the influence of dietary fat on breast cancer. There are as yet insufficient data from such studies to indicate whether decreasing the level of fat in the diet will reduce the risk of breast cancer. The studies have shown, however, that women given dietary counselling will reduce their dietary fat intake and remain on a low-fat diet for extended periods of time (34-36), although it would be desirable to extend this evidence to a broader socioeconomic group. In addition to studies on women at high risk of breast cancer, efforts are being made to determine whether a low-fat diet can help prevent recurrence in cancer patients (37).

Discussion

In attempting to decide whether dietary fat has a significant influence on breast cancer, it is important to consider why cohort studies and case-control studies have not supported this association as strongly as the inter-country comparisons. Various suggestions have been made to account for these differences (38-42).

For intercountry studies, dietary fat intake is normally estimated from disappearance data (43). This is a relatively crude method but when expressed as per cent of total calories, the results give a reasonable approximation to those obtained by more rigorous methods (44). The estimated intakes for different countries cover a relatively wide range from less than 10% to more than 40% of total calories. Although individuals in any given country may differ considerably in their fat intake, there will probably be relatively little overlap between countries with markedly different average intakes.

In cohort and case-control studies, dietary fat intake is commonly esti-

mated from diet records provided by individuals. This method is also rather inaccurate, particularly when it is used to estimate past dietary intakes. Furthermore, because the range covered in such studies is usually much less than for intercountry studies, the probability of overlap between the groups being compared is much greater.

Data on breast cancer incidence and mortality are probably much better for some countries than for others and this could introduce errors in the intercountry studies. This is not likely to be a problem in cohort and case-control studies, Nevertheless, a country such as Japan, which maintains good records on cancer incidence and mortality, has less breast cancer as well as a lower fat intake than Western industrialized countries.

Case-control studies have been widely used to study effects of dietary fat on breast cancer, but it appears that they may not be well-suited for studying effects on cancer promotion, which is the stage of carcinogenesis thought to be influenced by dietary fat. In such studies the cases are preselected, and because they have already developed cancer, they must have had adequate initiation as well as promotion for this to occur. The controls have not developed cancer and it is not possible to say whether this is because of lack of initiation or promotion. Since only about one woman in ten develops breast cancer, even in countries with the highest rates, a large proportion if controls selected at random would not be expected to develop the disease even on a high-fat diet. This could be due to inadequate initiation or lack of genetic susceptibility. On the other hand, cases consuming a lower fat diet may have developed breast cancer because of greater exposure to initiating stimuli or higher genetic susceptibility.

Cohort studies and intercountry studies do not suffer from this disadvantage because the cases are not preselected. In comparing the populations of two different countries, it seems reasonable to assume that each population will contain many individuals who are unlikely to develop breast cancer under any circumstances, whereas somewhat similar proportions of the populations of each country have increased susceptibility so that their likelihood of developing cancer depends on their degree of exposure to promoting agents. It is thus possible in such comparisons to observe the effects of promoting agents even though individual members of the population vary greatly in their susceptibility to cancer as a result of their inherent genetic characteristics and/or exposure to mutagens and carcinogens.

One of the problems in all types of epidemiological studies is the complication of confounding factors. It is particularly difficult, for example, to dissociate effects of dietary fat from those related to caloric intake, since high-fat diets are energy-rich and there is a strong positive correlation between fat intake and caloric intake (4). Thus, it has been suggested that the observed effects of dietary fat on carcinogenesis are primarily due to differences in caloric intake (45,46). Experiments on animals have demonstrated a requirement for n-6 essential fatty acids in the promotion of mammary cancer by dietary fat (47), but the effect also seems to depend on the level of dietary fat (48) and this may be related to caloric intake. The feasibility trials with low-fat diets in women (34,35) have shown that caloric intake decreases as the level of dietary fat is reduced, perhaps because of the more bulky nature of the low-fat diets, and this may be a more practical way of reducing caloric intake than restricting the intake of a high-fat diet.

It is noteworthy that Willett *et al.* (49) found a positive correlation between dietary fat and colon cancer in

the same cohort that failed to show a relationship with breast cancer (17). In studies on migrants and in time-trend studies, the incidence of colon cancer also tends to change more rapidly than does than of breast cancer (16). The reasons for this difference are not known, but one possibility is that breast cancer has a longer latent period than colon cancer, and that dietary intake during an earlier time period is more important for breast cancer. Evidence that breast cancer is influenced by factors such as age of menarche and age at first pregnancy is reason for thinking that breast cancer may often be initiated at a relatively young age (50,51).

More credence could be given to a role for dietary fat in breast cancer by providing a mechanism that could explain how its effects are mediated. Numerous mechanisms have been suggested, including effects on sex hormones and their receptors, on prostaglandins, on lipid peroxidation, and on membrane fluidity and cell-cell interactions (52,53). Another recently proposed mechanism is based on evidence that the adipose tissue of the mammary gland has a marked influence on growth and proliferation of the epithelial tissue in which cancers arise (54). Because adipose tissue is the major site of energy storage, it will tend to reflect differences in energy balance more generally than overall body weight. Changes in the amount and composition of mammary adipose tissue resulting from differences in dietary fat may thus affect mammary tumorigenesis. This theory could also help to explain effects of other dietary factors as well as effects of caloric restriction and exercise on mammary cancer (55-57).

References

1. National Research Council, Committee on Diet, Nutrition, and Cancer. Diet, Nutrition, and Cancer. Washington, DC: National Academy Press, 1982.
2. Tannenbaum A. The genesis and growth of tumors. III Effects of a high-fat diet. Cancer Res 1942; 2: 468-75.
3. Tannenbaum A. Nutrition and cancer. In: Homburger, F. ed. The Physiopathology of cancer. Ed. 2. New York: Hoeber-Harper, 1959: 517-62.
4. Carroll KK, Khor HT. Dietary fat in relation to tumorigenesis. Prog Biochem Pharmacol 1975; 10: 308-53.
5. Cohen LA. Dietary fat and mammary cancer. In: Reddy BS, Cohen LA. eds. Diet, Nutrition, and Cancer: A Critical Evaluation. Vol. I. Macronutrients and Cancer. Boca Raton, FL: CRC Press, 1986:77-100.
6. Freedman LS, Clifford C, Messina M. Analysis of dietary fat, calories, body weight, and the development of mammary tumors in rats and mice: a review. Cancer Res 1990; 50: 5710-9.
7. Angres G, Beth M. Effect of dietary constituents on carcinogenesis in different tumor models. An overview from 1975 to 1988. In: Alfin-Slater RB, Kritchevsky D. eds. Human Nutrition. A Comprehensive Treatise, Vol. 7, Cancer and Nutrition. New York: Plenum Press 1991; 337-485.
8. Carroll KK. Lipids and carcinogenesis. J Environ Pathol Toxicol 1980; 3(4): 253-71.
9. Carroll KK, Gammal EB, Plunkett ER. Dietary fat and mammary cancer. Can Med Assoc J 1968; 98: 590-4.
10. Carroll KK. Experimental evidence of dietary factors and hormone-dependent cancers. Cancer Res 1975; 35: 3374-83.

11. National Research Council, Committee on Diet and Health. Diet and health: implications for reducing chornic disease risk. Washington, DC: National Academy Press, 1989.

12. Cohen LA. Symposium on Lipids in Cancer. Introduction. Lipids 1992; in press.

13. Prentice RL, Sheppard L. Validity of international, time trend, and migrant studies of dietary factors and disease risk. Prev Med 1989; 18: 167-79.

14. McMichael AJ, Giles GC. Cancer in migrants to Australia: extending the descriptive epidemiological data. Cancer Res 1988; 48: 751-6.

15. Hirayama T. Diet and cancer. Nutr Cancer 1979; 1(3): 67-81.

16. Willett W. The search for the causes of breast and colon cancer. Nature 1989; 338: 389-94.

17. Willett WC, Stampfer MJ, Colditz GA, Rosner BA, Hennekens CH, Speizer FE. Dietary fat and the risk of breast cancer. N Engl J Med 1987; 316: 22-8.

18. Jones DY, Schatzkin A, Green SB, *et al.* Dietary fat and breast cancer in the National Health and Nutrition Examination Survey I. Epidemiologic follow-up study. J Natl Cancer Inst 1987; 79: 465-71.

19. Knekt P, Albanes D, Seppanen R *et al.* Dietary fat and risk of breast cancer. Am J Clin Nutr 1990; 52: 903-8.

20. Howe GR, Friedenreich CM, Jain M, Miller AB. A cohort study of fat intake and risk of breast cancer. J. Natl Cancer Inst 1991; 83: 336-40.

21. Iscovich JM, Iscovich RB, Howe G, Shiboski S, Kaldor JM. A case-control study of diet and breast cancer in Argentina. Int J Cancer 1989; 44: 770-6.

22. Rohan TE, Cook MG, Potter JD, McMichael AJ. A case-control study of diet and benign proliferative epithelial disorders of breast. Cancer Res 1990; 50: 3176-81.

23. Brisson J, Verrault R, Morrison AS, Tennina S, Meyer F. Diet, mammographic features of breast tissue, and breast cancer risk. Am J Epidemiol 1989; 130: 14-24.

24. Yu S-Z, Lu R-F, Xu D-D, Howe GR. A case-control study of dietary and nondietary risk factors for breast cancer in Shanghai. Cancer Res 1990; 50: 5017-21.

25. Ewertz M, Gill C. Deitary factors and breast-cancer risk in Denmark. Int J Cancer 1990; 46: 779-84.

26. Richardson S, Gerber M, Cen_e S. The role of fat, animal protein and some vitamin consumption in breast cancer: a case control study in Southern France. Int J Cancer 1991; 48: 1-9.

27. Katsouyanni K, Willett W, Trichopoulos, D, *et al.* Risk of breast cancer among Greek women in relation to nutrient intake. Cancer 1988; 61: 181-5.

28. Toniolo P, Riboli E, Protta F, Charrel M, Chappa APM. Calorie-providing nutrients and risk of breast cancer. J Natl Cancer Inst 1989; 81: 278-86.

29. Van't Veer P, van Leer EM, Rietduk A, *et al.* Combination of dietary factors in relation to breast-cancer occurrence. Int J Cancer 1991; 47: 649-53.

30. Zaridze D, Lifanova Y, Maximovitch D, Day NE, Duffy SW. Diet, alcohol consumption and reproductive factors in a case-control study of breast cancer in Moscow. Int J Cancer 1991; 48: 493-501.

31. Lee HP, Gourley L, Duffy SW, Esteve J, Lee J, Day NE. Dietary effects on breast-cancer risk in

Singapore. Lancet 1991; 337: 1197-200.

32. Pryor M, Slattery ML, Robinson LM, Egger M. Adolescent diet and breast cancer in Utah. Cancer Res 1989; 49: 2161-7.

33. Howe GR, Hirohata T, Hislop TG, *et al.* Dietary factors and risk of breast cancer: combined analysis of 12 case-control studies. J Natl Cancer Inst 1990; 82: 561-9.

34. Boyd NF, Cousins M, Beaton M, *et al.* Clinical trial of low-fat, high-carbohydrate diet in subjects with mammographic dysplasia: report of early outcomes. J Natl Cancer Inst 1988; 80: 1244-8.

35. Henderson MM, Kushi LH, Thompson DJ, *et al.* Feasibility of a randomized trial of a low-fat diet for the prevention of breast cancer: dietary compliance in the Women's Health Trial Vanquard Study. Pre Med 1990; 19: 115-33.

36. Holm LE. Nutritional intervention studies in cancer prevention. Med. Oncol. Tumor Pharmacother 1990; 7: 209-15.

37. Wynder EL, Morabia A, Rose DP, Cohen LA. Clinical trials of dietary intervention to enhance cancer survival. Prog Clin Biol Res 1990; 346: 217-29.

38. Goodwin PJ, Boyd NF. Critical appraisal of the evidence that dietary fat intake is related to breast cancer risk in humans. J Natl Cancer Inst 1987; 79: 473-85.

39. Freudenheim JL, Marshall JR. The problem of profound mismeasurement and the power of epidemiological studies of diet and cancer. Nutr Cancer 1988; 11: 243-50.

40. Prentice RL, Kakar F, Hursting S, Sheppard L, Klein R, Kushi LH. Aspects of the rationale for the Women's Health Trial. J Natl Cancer Inst 1988; 80: 802-14.

41. Hegsted DM. Errors of measurement. Nutr Cancer 1989; 12: 105-7.

42. Hebert JR, Kabat GC. Distribution of smoking and its association with lung cancer: implications for studies on the association of fat with cancer. J Natl Cancer Inst 1991; 83: 872-4.

43. Food and Agriculture Organization of the United Nations. Food Balance Sheets 1975-77 Average and Per Caput Food Supplies, 1961-65 Average, 1967 to 77. Rome: FAO, 1980.

44. Carroll KK. Experimental studies on dietary fat and cancer in relation to epidemiological data. In: Ip C, Birt DF, Rogers AE, Mettlin C. eds. Prog. Clin. Biol. Res. Vol. 222, Dietary Fat and Cancer, New York: Alan R. Liss, Inc. 1986: 231-48.

45. Pariza MW. Fat, calories, and mammary carcinogenesis: net energy effects. Am J Clin Nutr 1987; 45: 261-3.

46. Kritchevsky D. Nutrition and breast cancer. Cancer 1990; 66: 1321-5.

47. Carroll KK, Hopkins GJ, Kennedy TG, Davidson MB. Essential fatty acids in relation to mammary carcinogenesis. Prog Lipid Res 1981; 20: 685-90.

48. Ip C. Fat and essential fatty acid in mammary carcinogenesis. Am J Clin Nutr 1987; 45: 218-24.

49. Willett WC, Stampfer MJ, Colditz GA, Rosner BA, Speizer FE. Realtion of meat, fat, and fibre intake to the risk of colon cancer in a prospective study among women. N Engl J Med 1990; 323: 1664-72.

50. De Waard F, Trichopoulos D. A unifying concept of the aetiology of breast cancer. Int J Cancer 1988; 41: 666-9.

51. Carroll KK, Jacobson EA, James

KA. Role of dietary fat in carcinogenesis. In: Kabara JJ, ed. The Pharmacological Effects of Lipids III. Champaign, IL: Am. Oil Chemists' Soc. 1989: 129-35.

52. Cohen LA. Dietary fat and mammary cancer. In: Reddy BS, Cohen LA. eds. Diet, Nutrition, and Cancer: A Critical Evaluation. Vol. I. Macronutrients and Cancer. Boca Raton, FL:CRC Press 1986: 77-100.
53. Welsch CW. Enhancement of mammary tumorigenesis by dietary fat: review of potential mechanisms. Am J. Clin Nutr 1987; 45: 192-202.
54. Carroll KK, Parenteau HI. A proposed mechanism for effects of diet on mammary cancer. Nutr Cancer 1991; 16: 79-83.
55. Cohen LA, Choi K, Wang C-X. Influence of dietary fat, caloric restriction, and voluntary exercise on N-nitrosomethylurea-induced mammary tumorigenesis in rats. Cancer Res 1988; 48: 4276-83.
56. Simopoulos AP. Energy imbalance and cancer of the breast, colon and prostate. Med Oncol Tumor Pharmacother 1990; 7: 109-20.
57. Weindruch R, Albanes D, Kritchevsky D. The role of calories and caloric restriction in carcinogenesis. Hematol Oncol Clin North Am 1991; 5: 79-89.

Proc 6th ACN 1991: 213

Nutrition initiator and promotor on liver carcinogenesis

Panata Migasena

Department of Tropical Nutrition and Food Science, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand

Abstract

Liver Carcinomas both hepatoma and Cholangiocarcinoma are rather commonly found in Thailand. Food habit of eating raw fish, nitrate, nitrite an dnitroso-compounds not only as contaminated in food but also nitrosation in human body are also studies for a probable carcinogen in the carcinogenesis. Serum bile acids and bile salts and also serum proteins especially the fast reacting fraction in alpha and beta range of electrophoretic pattern are also studied not only in term of carcinogenic promotor but also as an indicator of the host response to cell damage and also the process of cell regeneration in malnutritional state.

The hypothesis on carcinogenesis of both hepatocellular carcinoma and cholangiocarcinoma in Thailand can be proposed. The malignant transformation begins primarily with the cell injury. Hepatitis B virus or food toxicants cause liver cell necrosis whereas the liver flukes and their eggs irritate and damage the cell lining of bile ducts. During the process of regeneration, with superimposed malnutrition, the hyperplasia and proliferation of these damaged cells may be more vulnerable to nitrosamine which contaminated in food or formated in the gastrointestinal tract due to the high content of nitrate, nitrite and amines in food. High level of bile acids and bile salts resulted from cholestasis may play an important role as a promotor of nitrosamine carcinogenic transformation. Furthermore, the host response of malnourished individuals in both hepatitis and opisthorchiasis may also play a possible role in carcinogenesis of these liver carcinomas.

Proc 6th ACN 1991: 214-215

Natural carotenoids and cancer

H Nishino

Department of Biochemistry, Kyoto Prefectural University of Medicine, Kawaramachi-Hirokoji, Kamigyoku, Kyoto 602, Japan

Epidemiological investigations have shown that cancer risk is inversely related to the consumption of green and yellow vegetables. β-Carotene which is known to have the highest potency to serve as pro-vitamin A and which is present in abundance in green and yellow vegetables, has been proposed to be one of the key principles to prevent cancer. In fact, β-carotene was proved experimentally to prevent carcinogenesis induced by chemicals or viruses. β-Carotene is one of the most widespread natural carotenoids, but it is often associated with other carotenoids, such as α-carotene, α-carotene, lycopene and so on. Therefore, it is of interest to investigate the biological activity of these various kinds of carotenoids more extensively.

Recently, we found that palm oil-derived natural carotene which consists of 60% β-carotene, 30% α-carotene and 10% others, remarkably suppressed the promotional stage of carcinogenesis. In this context, we compared the anti-tumour-promoting activity of α-carotene with that of β-carotene. Since the lung is suggested epidemiologically to be a possible target organ for carotenoids to suppress carcinogenesis, it is of particular interest to investigate the effect of these carotenoids on the lung carcinogenesis. In this study, we examined the effect of α- and β-carotene on the tumour-promoting action of glycerol in 4NQO-initiated mice. The animals used were 6-week-old ddY male mice. Initiation of carcinogenesis was performed by a single subcutaneous injection of 0.3 mg of 4NQO on the first experimental day. Glycerol, a tumour promoter, was dissolved in water and 10% solution was given as drinking water *ad libitum* from the beginning of experimental week 5. α- and β-carotene (at the concentration of 0.05%) or vehicle was mixed in drinking water. Mice were killed at week 30 by cervical dislocation. At autopsy, the lungs were fixed via intratracheal instillation of 10% formaldehyde. After separation of each pulmonary lobe, the number of induced tumours was counted under a microscope.

Administration of α-carotene resulted in the decrease of the mean number of tumours per mouse to about 23% of the control group ($p < 0.01$, Student's t-test). β-Carotene also showed the tendency to suppress the lung tumour formation, but the effect was not statistically significant. Thus, it is apparent that α-carotene has more effective anti-tumour-promoting activity than β-carotene in lung carcinogenesis.

The higher potency of α-carotene than β-carotene to suppress tumour

promotion was confirmed by other experimental system of two-stage carcinogenesis *in vivo;* i.e., α-carotene was proved to have stronger effect than β-carotene to suppress the promoting activity of TPA on skin carcinogenesis in DMBA-initiated mice.

Since the vitamin A activity of α-carotene is about half of that of β-carotene, it is unlikely that the anti-carcinogenic effect of these carotenoids reflects their vitamin A activity. The mechanism of the anti-tumour-promoting effect of α- and β-carotene remains to be elucidated.

From these results, the more extensive investigations of biological activity of not only β-carotene but also of α-carotene and other kinds of carotenoids seem to be important to evaluate the anti-carcinogenic effect of natural carotenoids in daily foods, which might play significant role to reduce the incidence of human cancer and might be useful for the purpose of cancer chemoprevention.