Human health and nutrition: How isotopes are helping to overcome"hidden hunger"

In increasing ways, stable and radioactive isotopes are contributing to research of serious nutritional problems affecting human health

by
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and
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Health authorities in all countries are concerned about the nutrition of their population.

In the industrialized world, major concerns are related to what has been called "over nutrition". With higher affluence and urbanization, diets tend to become higher in energy and fat, especially saturated fat. They also have less fibre and complex carbohydrates, and more alcohol. These and other risk factors are leading to increased incidence of obesity, hypertension, cardiovascular diseases, diabetes mellitus, osteoporosis, anaemia and some cancers, with immense social and health care costs.

For developing countries, the problems chiefly lie on the other end of the spectrum. "Under nutrition", or malnutrition, is the principal enemy, mainly of poor people who experience the most widespread and severe effects of malnutrition.

Some statistics are truly alarming. More than 780 million people — 20% of the developing world — are chronically undernourished. About 190 million children under five years of age, including more than 150 million in Asia and 27 million in Africa, suffer from protein-energy malnutrition. Every day, 40 000 children under the age of five die, and malnutrition is a major contributing factor. Some 2000 million people in more than 100 developing countries suffer from micronutrient deficiencies that can lead to blindness, mental retardation, and even death.

Many problems are not new — indeed, most of them have been recognized for years. Their severity varies widely from one country to another, and also over time. Some countries have observed significant decreases in diet-related mortality in recent years; many others, however, show substantial increases. *(See graphs, page 20.)*

Nutritional problems underlying these trends (particularly in developing countries) are generally not related to an absolute deficiency of food — to overt hunger. In most cases, they are caused by insufficient *quality* of food, or lack of variety, leading to deficiencies of vitamins and essential minerals. Because many effects are not immediately obvious to the naked eye, the World Health Organization (WHO) has coined the term "hidden hunger" to describe these problems.

In a number of ways, the work of the IAEA is contributing to efforts directed at overcoming hidden hunger and other nutrition problems. The rationale for the IAEA's involvement is twofold. First, adequate nutrition is an essential component of any strategy for improving *health*, and the IAEA's Statute specifically identifies "enlarging the contribution of atomic energy to peace, *health* and prosperity" as the major objective of programmes. Second, isotope techniques have a wide variety of applications — some of them unique — for targeted research in human nutrition, for assessing nutritional status, and for monitoring the effectiveness of nutritional intervention programmes. *(See table, page 21.)*

This article provides a brief overview of these techniques and their main applications in areas of human nutrition. It further illustrates how the IAEA's programmes are directed towards helping to solve specific nutrition problems, particularly those affecting women and children in developing countries.

Micronutrient malnutrition: Vitamin and mineral deficiencies

Overview of the problem. Micronutrients — vitamins and minerals — play a wide role in

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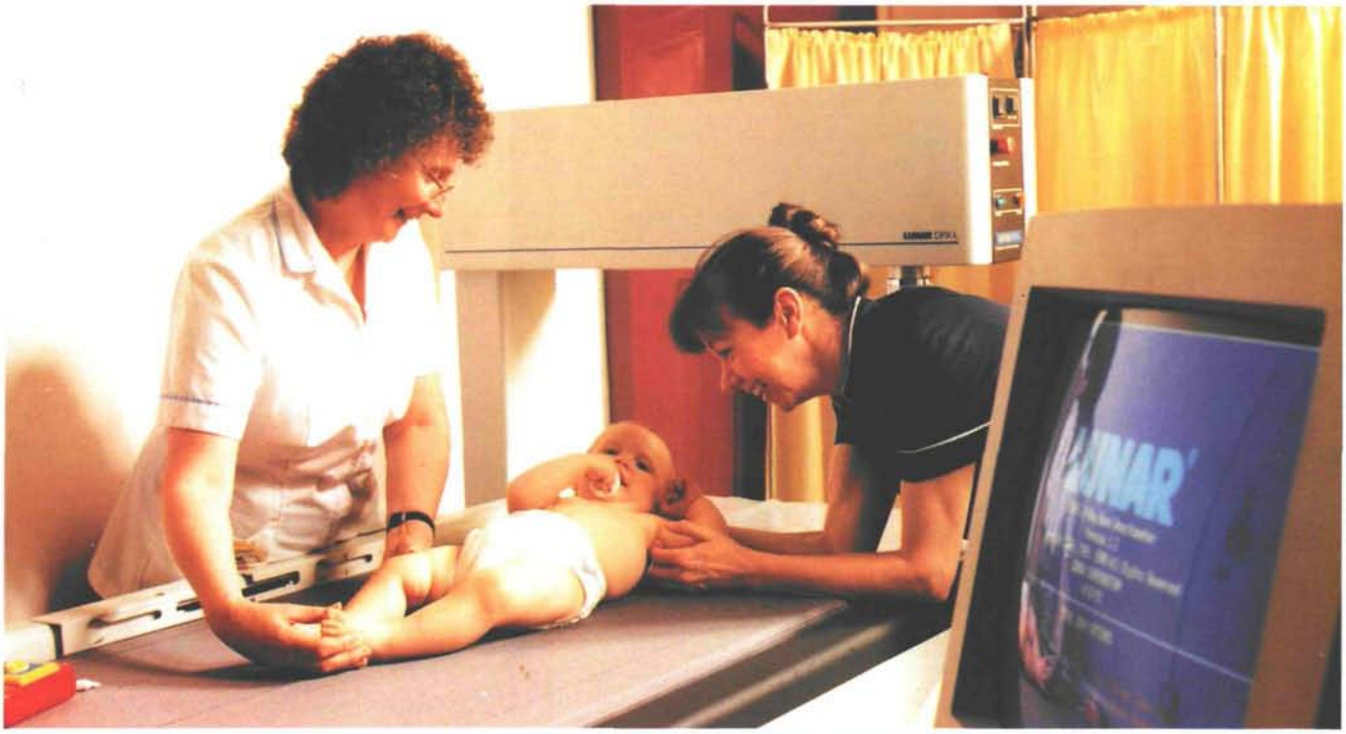
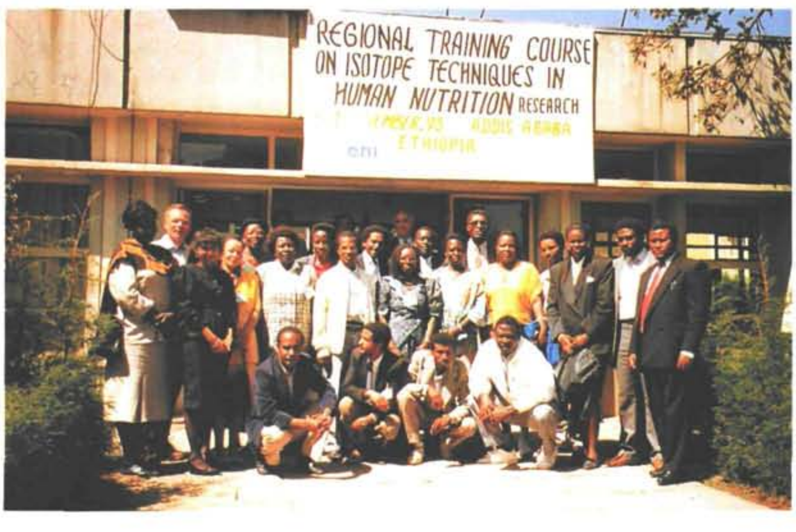


Millions of men, women, and children around the world are undernourished for one reason or another. Through various programmes, the IAEA is supporting work to study nutritional problems and improve the health of people, often placing particular emphasis on maternal and child nutrition. The work includes targeted research projects, technical assistance, and training courses for scientists — such as the one shown at right in Addis Ababa, Ethiopia in November 1993 — on the use of nuclear and related techniques for studying aspects of malnutrition and health. Since 1990, the IAEA has supported nutrition programmes in more than 50 countries. *(Credits: AEA Technology; Schytte/WHO; R. Parr, IAEA)*

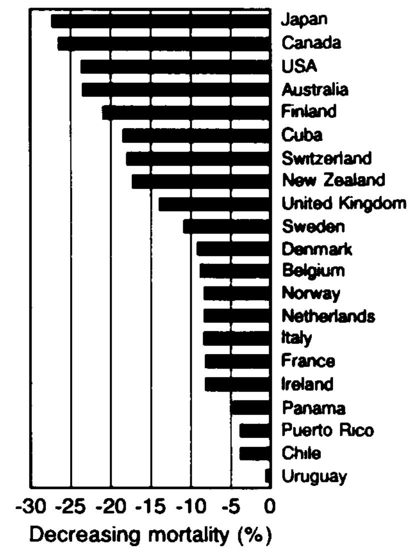


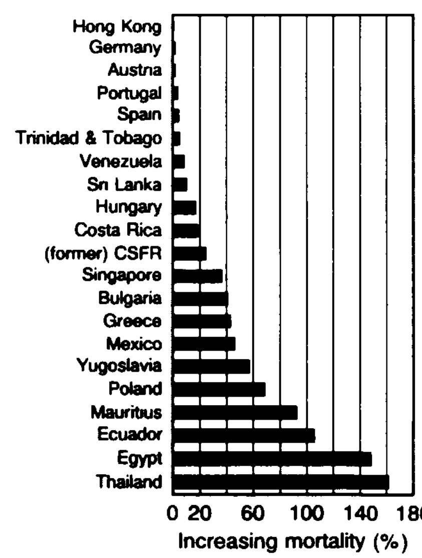
World Declaration on Nutrition

One of the most significant recent events in human nutrition was the International Conference on Nutrition (ICN) organized by the World Health Organization (WHO) and Food and Agriculture Organization (FAO) of the United Nations in Rome at the end of 1992. For the first time in history, governments acting in an international forum were asked to think beyond the still-present problems of hunger and survival and to focus squarely on nutrition and health. The outcome was a "World Declaration on Nutrition". It was adopted by government ministers and senior policy makers from more than 150 countries, together with representatives of non-governmental organizations. Selected quotations from this declaration appear below:

- the nutritional well-being of all people is a pre-condition for the development of societies ... it should be a key objective of programmes in human development and at the centre of our socio-economic development plans and strategies
- globally there is enough food for all ... inadequate access is the main problem
- access to nutritionally adequate and safe food is a right of each individual
- there is a high prevalence and increasing numbers of malnourished children under five years of age in parts of Africa, Asia and Latin America and the Caribbean ... particular emphasis should be given to their nutrition problems
- more than 2000 million people, mostly women and children, are deficient in one or more micronutrients
- nutrition goals of the Fourth United Nations Development Decade include .. reducing malnutrition and mortality among children substantially
- nutrition goals of the World Summit for Children (to be reached by the year 2000) include: reduction in severe as well as moderate malnutrition among under-5 children by half of 1990 levels; reduction of iron deficiency anaemia in women by one-third of the 1990 levels; virtual elimination of iodine deficiency disorders; virtual elimination of vitamin-A deficiency and its consequences; and institutionalization of growth promotion and its regular monitoring in all countries by the end of the 1990s
- basic and applied scientific research, as well as food and nutrition surveillance systems, are needed to more clearly identify the factors that contribute to the problems of malnutrition and the ways and means of eliminating these problems, particularly for women, children and aged persons
- the governing bodies of FAO, WHO ... and other concerned international organizations should ... decide on ways and means of giving appropriate priority to their nutrition-related programmes and activities aimed at ensuring, as soon as possible, the vigorous and coordinated implementation of activities recommended in the World Declaration and Plan of Action for Nutrition ... this would include, as appropriate, increased assistance to the member countries.

Change in mortality rates due to diet-related non-communicable diseases





Note: Data applies to subjects 65 years and over, between 1960-64 and 1985-89 in 42 countries.

Source: WHO

health and development. Besides preventing specific disorders, they protect the lives of mothers and children, stimulate cognitive development, help protect against infections and improve people's capacity for work.

Micronutrient deficiencies can cause harm from the moment of conception because they influence the regulation of growth and other physiological processes. Deficiencies can lead to a vicious cycle that takes more than one generation to correct: malnourished mothers give birth to children who carry the effects into adulthood and, if female, into the next generation.

Iron deficiency is the most common nutritional deficiency in the world today. In infancy and childhood, it can impair learning and the ability to resist disease. The lethargy it induces in adults reduces their capacity to work and to

Examples of IAEA support to human nutrition programmes (1990-1994)

	Research & technical assistance*	Training & seminars**
Argentina	1	
Australia	2	
Bangladesh	4	1
Bolivia	1	
Brazil	2	2
Cameroon	1	4
Canada	2	1
Chile	3	2
China	3	2
Czech Republic	1	
Ethiopia		4
Finland	1	
France	1	
Germany	1	
Ghana		2
Guatemala	2	
Hungary	1	
India	6	20
Indonesia	2	1
Iran	1	
Italy	1	
Jamaica	2	
Kenya		4
Madagascar		1
Malaysia	3	2
Mauritius		1
Mexico	1	
Myanmar	1	2
Netherlands	1	
Nepal		1
Nigeria		2
Pakistan	2	1
Papua New Guinea	1	
Peru	2	1
Philippines	1	2
Poland	1	1
Portugal	1	
Romania	1	1
Senegal		2
Sierra Leone		2
Slovenia	2	
Spain	1	
Sri Lanka	1	1
Sudan	1	2
Tanzania		2
Thailand	1	2
Turkey	1	
Uganda		1
United Kingdom	5	2
United States	11	4
USSR (former)	1	
Venezuela	1	1
Zaire		1

* Number of projects (including research agreements)
** Number of participants/trainees

take care of families and homes. More than 2000 million people worldwide are anaemic or iron deficient, most of them in developing countries. The loss of menstrual blood makes women of child-bearing age particularly vulnerable. Anaemia contributes to high maternal mortality rates, low birth weight, and increased infant mortality.

Iodine deficiency affects production of the thyroid hormones that govern the development and function of the brain and nervous system and regulate body heat and energy. A low level of thyroid hormones can reduce both physical and mental capacity. In pregnant women, iodine deficiency can cause miscarriages and still births. It may lead to irreversible brain damage in the foetus or newborn and cause mental retardation in children. It is estimated that more than 1000 million persons live in areas at risk of iodine deficiency. Two hundred million have goitre — an enlargement of the thyroid gland in the neck — and 26 million are mentally retarded as a result of the deficiency.

Vitamin-A deficiency is the most common cause of preventable childhood blindness, reduces the effectiveness of the immune system, and retards growth and development. At least 40 million preschool children are deficient in vitamin-A, and among them 13 million already have some eye damage. Every year, up to half a million preschool children go blind, partially or totally, from vitamin-A deficiency. Approximately two-thirds of them die within a few months of losing their sight. A lack of vitamin-A and other essential nutrients also makes children

Overview of selected isotope techniques in human nutrition studies

Technique	Application
Radioisotope tracer study (with sample counting)	Body composition (tritium labelled water) *in vivo* study of iron uptake and bioavailability (iron-59/iron-55) *in vitro* study of iron dialyzability (iron-59)
Radioimmunoassay	Iron status (based on serum ferritin) Iodine status (based on T_3, T_4, TSH)
Nuclear analytical techniques (e g NAA)	Trace element content of foods, diets, and human tissues
Whole body counting	Body composition (lean body mass — potassium-40) Uptake, bioavailability of essential micronutrients, e.g iron (iron-59) and zinc (zinc-65)
In vivo neutron activation analysis (NAA)	Body composition (total body nitrogen, calcium, etc.)
Stable isotope tracer study	Body composition (deuterium labelled water) Substrate metabolism (carbon-13 and nitrogen-15 labelled amino acids, fats, etc.) Energy expenditure (deuterium and oxygen-18 labelled water) Uptake and bioavailability of essential micronutrients, e.g iron, zinc and vitamin-A using appropriate stable isotopes

more vulnerable to the severe consequences of diseases such as measles, diarrhoea and respiratory infections. Some studies indicate that even moderate levels of vitamin-A deficiency can lead to stunted growth, increased severity of infection, higher death rates in children, and may increase mother-to-fetus transmission of the HIV virus in HIV-positive women.

Isotope techniques in studies of micronutrient malnutrition

Many micronutrients, both vitamins and trace elements, that are of crucial importance in human nutrition can be studied with the use of isotope techniques.

Iron. Of fundamental importance in any study of iron nutrition is the actual uptake of iron by the body (e.g. from a foodstuff or meal) in a metabolically active form. Much is already known about this. For example, the amount absorbed depends very much on the source of the iron (whether from meat or from vegetables) and on the presence of other substances such as vitamin-C (from fruit and some vegetables), phytate (from some cereal products) and tannin (from tea). However, much still needs to be learned about the interactions between these components, and about ways to optimize iron absorption by appropriate selection of locally available foodstuffs and by the use of food processing methods, such as fermentation and germination.

Isotope techniques provide the only direct way for measuring iron uptake and bioavailability and are correctly regarded as a kind of "gold standard" for iron studies in humans. The most common form of the method is based on incorporation of radioactive iron isotopes (iron-55 and iron-59) into red blood cells following extrinsic labelling of the food or diet to be tested and feeding it to selected test subjects. Blood samples are taken over a period of 2-4 weeks and processed for counting with a liquid scintillation counter. Alternatively, iron-59 can be measured with a whole body counter. More recently, in some countries, the use of stable isotopes (iron-54, -57, and -58) measured by mass spectrometry has come to be regarded as a preferable technique because of the absence of a radiation dose, which therefore permits studies to be made on children and pregnant women.

A useful alternative procedure — though less accurate — is one that can be done without the need to resort to using test subjects. The foodstuff to be tested is subjected to an *in vitro* laboratory digestion under conditions that mimic what is happening in the stomach. The release of iron in low molecular weight species is estimated with the help of an iron-59 tracer following dialysis through a synthetic membrane. This is a very useful rapid screening tool.

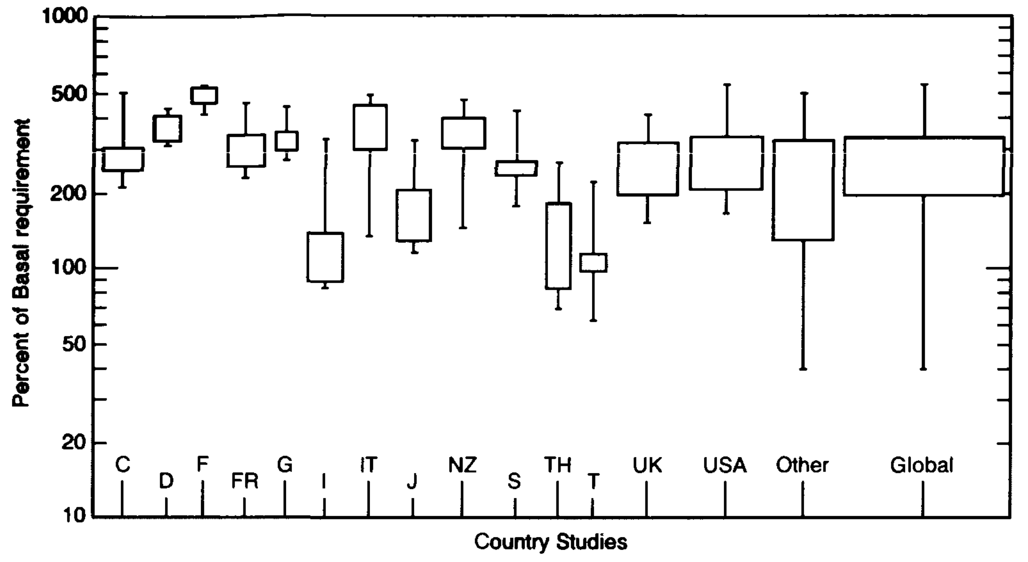
Isotope methods are also useful for assessing the iron status of individuals and populations based on measurements of serum ferritin. Low serum ferritin reflects depleted body iron stores and is the most specific finding for iron deficiency. Immunoassay — either radioimmunoassay (RIA) or an enzyme-based assay (ELISA) — is the only technique currently available for measuring ferritin.

Iodine. Areas of endemic iodine deficiency are usually identified from measurements of urinary iodine excretion (using non-nuclear techniques). However, useful additional information on the nutritional iodine status of a person or population can sometimes be obtained by looking at the levels of thyroid-related hormones in blood serum. Iodine deficiency of moderate to severe degree results in changes in the pattern of secretion, and therefore serum concentrations, of thyroid hormones. Immunoassay is the technique of choice for such determinations. It relies on the use of antibodies as specific binding agents to detect a diversity of analytes (in this case, thyroid-related hormones such as T_3, T_4 and TSH). A high degree of specificity, sensitivity and robustness is provided. RIA and ELISA are the two applicable forms of immunoassay. For centres that already have access to RIA, this technique is often preferred because it is more robust; also, as shown in several IAEA programmes, it can be made very cost-effective by the use of bulk reagents, some of which may be locally produced.

Vitamin-A. Isotope methods for studying vitamin-A are not yet as well developed as for the other micronutrients just mentioned. However, there is no doubt that they will have uniquely valuable applications in assessing vitamin-A status, e.g. from measurements of plasma clearance of a test dose of isotopically labelled retinol. For human studies, deuterium is usually chosen as the isotopic label.

Large-scale programmes have already been implemented by UNICEF, WHO, and other agencies to prevent vitamin-A deficiency disorders. They include supplementation with vitamin-A, dietary modification to increase intake of vitamin-A (which can be expensive) or of its precursor, beta-carotene (which is from plant sources and can be less expensive), fortification of foods with vitamin-A, and breast-feeding programmes. Isotopic methods are under development which are expected to dramatically improve assessments of vitamin-A status in developing countries.

Dietary intakes of zinc: Overview of studies in various countries



The graph shows the distribution of dietary intakes of zinc in various countries expressed relative to the new WHO/FAO/IAEA basal requirements. The results indicate that only very few data on dietary intakes of trace elements are so far available from developing countries. In the few cases where such data are available, they indicate that dietary intakes of zinc in most developing countries are, at best, only marginally sufficient (and in some cases are actually deficient as judged by comparison with the basal requirements). Partly as a result of this kind of investigation, the possibility that zinc malnutrition may be relatively widespread is now coming to the attention of international bodies responsible for nutrition. It may be anticipated that, during the next few years, there will be a rapid growth in the number of studies of zinc nutrition in developing countries. Nuclear techniques are potentially able to play an important role in this work, and the IAEA is planning to start a new programme on this topic in 1996.

The countries presented are: Canada (C), Denmark (D), Finland (F), France (FR), Germany (G), India (I), Italy (IT), Japan (J), New Zealand (NZ), Sweden (S), Thailand (Th), Turkey (T), United Kingdom (UK) and United States (USA). Countries in the category "other" are Australia, Belgium, Brazil, China, Iran, Malawi, Morocco, Myanmar, Netherlands, Nigeria, Philippines, Poland, Spain, Sudan, Switzerland, the former USSR, and the former Yugoslavia. The "global" category refers to the total data set from all studies.

Other trace elements. Isotope techniques — particularly nuclear analytical methods such as neutron activation analysis (NAA) — are particularly useful for the study of trace elements in foods and diets. Of interest are *essential* trace elements such as copper, manganese, selenium, and zinc (in addition to the iron and iodine already mentioned), and *toxic* elements such as arsenic, cadmium, and mercury. In a recent IAEA-supported research programme in 16 countries, NAA was the technique of choice for 14 of the 24 elements of interest, and served as a quality control procedure for a further group of four elements.

IAEA programmes and plans in areas of micronutrient malnutrition. Since 1990, the IAEA has been supporting a co-ordinated research programme (CRP) in 11 countries on "Isotope-Aided Studies of the Bioavailability of Iron and Zinc from Human Diets". Its main focus has been to obtain critical information needed for planning and implementing national nutrition programmes on dietary diversification and modification, food fortification, and micronutrient supplementation, and in assessing the efficacy of intervention efforts.

Continuing work is foreseen, in collaboration with WHO. It is being done to obtain a better understanding of the quantitative relationships between the absorption of food iron from a meal and the amounts of the main food components that are known to affect iron bioavailability. (One simple example of the importance of these interactions is that drinking tea with a meal blocks iron absorption almost completely.)

It is also expected that the IAEA will support several technical co-operation projects in Africa and Latin America during 1995-96. Among other objectives, they will seek to develop iron-rich weaning foods for babies using local food products. A variety of *in vivo* and *in vitro* isotope techniques are needed for this work, using both radioactive and stable isotope tracers.

With respect to iodine *nutrition*, the IAEA has not yet directly supported work on this subject. However, many programmes have provided indirect support, particularly in relation to the use of RIA for the diagnosis of neonatal hypothyroidism (which is generally caused by nutritional iodine deficiency in the mother).

Several new IAEA programmes on vitamin-A malnutrition are planned. They include a CRP in 1995 to develop new methods for assessing vitamin-A status, to apply existing methods when feasible, and to develop new models for interpreting isotope kinetic data. Secondly, a new area of investigation will be supported which includes the production of foods intrinsically labelled with isotopes of carbon and hydrogen to assess the bioconversion of carotenoids under specific dietary and physiologic conditions. Thirdly, the IAEA will support the use of some techniques in a joint nutrition intervention project with WHO beginning late in 1994 or early 1995 in Latin America.

Concerning trace elements, the data generated through IAEA-supported research covering 25 study groups in 16 countries has already been used in the preparation of working documents for the WHO/FAO/IAEA Expert Consultation on Trace Elements in Human Nutrition. (A soon-to-be published report will propose new values for the dietary intakes of trace elements required to sustain good health.) The data also have served as input to a database on dietary intakes of 35 minor and trace elements in 47 different countries. *(See graph, page 23.)*

Special malnutrition problems of mothers and children

For some population groups — namely mothers and children — protein-related nutritional problems are especially serious. Operating in synergism with diarrhoeal, respiratory, and other infections, poor diets in early childhood lead to growth failure, delayed motor and mental development, impaired immunocompetence, and higher risks of complications and death from infectious disease.

While this form of malnutrition partially results from an insufficient amount of food, a major factor is inadequate dietary quality and diversity. Infection also contributes substantially to protein-energy malnutrition. It causes some anorexia, increases metabolic rates, and diverts protein and other important nutrients from maintenance and growth to processes involved in combatting infection.

In developing countries, poor children under 5 years of age suffer from five to ten episodes of infectious disease per year, as well as subclinical infections. The risk of dying from a given disease is doubled for mildly malnourished children and tripled for the moderately malnourished.

For women, deficiencies of protein and energy during child-bearing years increase maternal risk at childbirth, and lead to low birth-weights and to increased perinatal morbidity and mortality. More than 20 million low birth-weight children are born every year, more than 90% of them in developing countries. Most of these are due to maternal malnutrition.

Sustained access to adequate quantities of nutritious foods would certainly help solve the problems of under nutrition. However, this is not a goal which is immediately achievable. Before that becomes a reality, a key to developing interventions to solve these nutrition problems is the ability to make accurate nutritional assessments and to recommend foods which improve nutrition while making efficient use of scarce resources. Isotope techniques are uniquely and highly suitable for these applications.

Isotope techniques have been used extensively in industrialized countries to provide important information which has contributed substantially to improving understanding of protein nutrition for the past two decades and of energy requirements for the past decade. They are applicable for helping to design practical nutritional intervention programmes, and for monitoring the effectiveness of such programmes. The IAEA's nutrition programmes in the area of protein-energy nutrition aim to transfer established isotope and related technologies, with or without adaptations, to developing countries, as well as promote the development of new techniques and protocols. Work of this kind has expanded considerably since 1992 with the help of additional funding provided by the United States. The two groups of greatest interest in these programmes are mothers and children.

Malnutrition in mothers. Research from around the world has documented that nutrition programmes aimed at malnourished mothers and children lead to improvements in health and well-being. Furthermore, as has been demonstrated in Central America, appropriate nutritional supplements in one generation can have impact on subsequent generations. One of the more important questions in regard to maternal nutrition is nutrition during pregnancy, particularly with regard to weight gain during pregnancy. It is often assumed that mothers who gain relatively more weight during pregnancy will deliver healthier babies and reduce the risk of having low birth-weight infants.

Applications of isotope technologies in studies to improve pregnancy outcome. Maternal body composition during pregnancy — and its relation to dietary intake and pregnancy outcome — is assessed by measuring body composition prior to conception and comparing this with body composition during pregnancy and post partum. This information forms part of the basis of evaluations of nutrient requirements for pregnancy — a critical issue in developing countries.

The other area with broad practical implications concerns the energy requirements for pregnancy. Estimates jointly reported by the FAO, WHO, and United Nations University (UNU) are based on an accepted estimate of total energy needs for pregnancy of 335 MJ. However, this small increment in energy requirement observed for the whole of pregnancy is thought to be due to concomitant reductions in physical activity, particularly in women without access to adequate diets. In general, if the energy requirements of pregnancy *per se* are not met, the results may be either low birth-weight infants, reduced work capacity during pregnancy, reduced fat stores which may be needed as an energy source during lactation, and/or reduced physical activity. The IAEA remains involved in studies in developing countries in which body fat stores are measured using isotope techniques.

IAEA-supported maternal nutrition programmes. The IAEA has contributed in two important ways to improving maternal nutrition during pregnancy. The first was its joint support, with the International Dietary Energy Consultancy Group (IDECG), of a report on the scientific basis and practical application of the doubly labelled water (DLW) method for measuring energy expenditure.* Furthermore, the IAEA has supported several multi-centre and individual studies of energy expenditure during pregnancy. The results of some of these studies provide part of the basis of a reevaluation of dietary energy requirements which is being conducted by FAO, WHO, IDECG, and the UNU.

The DLW method, which was developed by Nathan Lifson and modified by investigators worldwide, is a form of direct calorimetry. It is based on the differential elimination of deuterium and oxygen-18 from body water subsequent to a loading dose of these stable isotopes. Once the two isotopes are administered, their fates are different; they are eliminated at different rates — deuterium only as water, and oxygen-18 as water plus carbon dioxide. The difference between the two elimination rates is therefore a measure of carbon dioxide production during the observation period, typically four to 21 days.

**The Doubly Labelled Water Method for Measuring Energy Expenditure: Technical Recommendations for Use in Humans.* This manual covers major theoretical and practical aspects of the method and has been distributed to researchers in 38 countries. Further information is available from the authors.

Measurement of the body's energy expenditure is important for several reasons. Specifically, it provides very useful information for a wide variety of assessments concerning nutritional interventions. For example, dietary supplements to previously undernourished children may increase the energy available not only for growth but also for activity, which could have great relevance in terms of school or athletic performance. In pregnant or lactating mothers, the drive to sustain pregnancy and lactation may reduce energy available for other functions, including physical activity.

In children with respiratory disorders such as allergies or cystic fibrosis, medications are prescribed which facilitate their breathing. However, as a secondary effect, the treatment may increase energy expenditure and therefore have an indirect and negative effect on weight gain.

Understanding the interactions between the various human functions that are energy-demanding is a key to providing adequate dietary intake. Meeting this need requires measurements of energy expenditure.

Malnutrition in children. For children with protein-energy malnutrition, the nutritional requirements exceed those of well-nourished children. This is because the need to replete weight deficits adds to the nutritional requirements for normal maintenance and growth. Because growth is one of the most universally applied indicators of nutritional status in children, deviations from normal patterns of growth can be analyzed to learn about the severity and remediation of under nutrition. Restoration of normal body weight and body composition through appropriate nutrition in undernourished children requires information about whether or not their body composition has been altered secondary to nutritional deficits.

One way to obtain this information is through anthropometry, a method in which measurements of weight, height, arm circumference, and skinfold thickness are used to estimate body composition. This method is only an estimate, however. Equations which relate the anthropometric measurements to body composition are based on specific population values, regarded as appropriate for the individual, which have been validated against more reliable measurements of body composition using isotopic and other methods.

Applications of isotope technologies in studies to improve child nutrition. Again, one widely used direct method is the measurement of total body water by deuterium and oxygen-18 dilution. Growth analysis is not only concerned with height and weight, but also includes evaluations of body composition.

Deuterium and oxygen-18 can be used without exposing the subjects to radiation and without sacrificing precision of measurements. The use of radioactive tracers (such as tritium) is not uniformly considered to be ethical in research involving children or women of child-bearing age, or in applications utilizing repeated measurements in the same person over a short period of time. Deuterium began to replace tritium as gas chromatography, infrared absorptiometry, and isotope ratio mass spectrometry technologies advanced and precision with these methods became acceptable. More recently, oxygen-18 has been used as a tracer to measure total body water because it avoids the exchange of the label with nonaqueous hydrogen in the body and thus the potential to overestimate the volume of body water. The most significant limitation to its wide use is cost, which is approximately 100 times more than deuterium.

IAEA-supported child nutrition programmes. The IAEA has contributed in some important ways to the improvement of dietary formulations for severely malnourished children through applications involving deuterium, oxygen-18, and carbon-13. Measurements of body composition, protein deposition, and energy expenditure were used in defining a dietary treatment for undernourished children which fosters substantial accelerations in weight gain without compromising the quantity of lean tissue. The result of using the dietary intervention was to reduce hospitalization time by 50%.

Particularly in children of developing countries, under nutrition and infection act synergistically to reduce nutrients available for growth, deplete energy reserves, and significantly increase morbidity and mortality. By better understanding the metabolic effects of infection in undernourished populations, we strengthen our ability to provide the appropriate foods for reducing morbidity and mortality. Stable isotope methods afford us this opportunity. Isotopic methods are being utilized in the new programmes to measure synthetic rates of specific nutrient transport proteins, and synthetic rates of proteins manufactured by the body in response to immunogenic stimuli. Both of these kinds of studies are currently being carried out by teams of scientists from developing and industrialized countries.

One team of investigators, for example, is working to find out how infection may alter children's dietary requirements for protein and amino acids. The work involves quantifying the relative impact of specific infections on protein metabolism and protein anabolism using amino acids labelled with carbon-13 and nitrogen-15. Isotopic enrichments are measured either by gas chromatography-mass spectrometry (GCMS), by combustion GCMS, or by isotope ratio mass spectrometry. The team is also assessing the impact of high altitude living on protein metabolism in undernourished children. They have developed and are validating a basic protocol for assessing rates of protein and amino acid metabolism in the field using non-invasive procedures that can be carried out under field conditions. The team intends to use the data in developing a food supplement that will most efficiently meet requirements for protein and specific amino acids, thereby resulting in the efficient utilization of nutrients for growth.

Nutrition and the elderly

Another population group heavily affected by nutritionally related problems is the elderly. A special concern in many countries is the disease known as osteoporosis. This serious bone disease of the elderly (particularly post-menopausal women) severely limits their quality of life and is placing an increasing burden on the health-care systems in many countries. It is characterized by low bone mass, and microarchitectural deterioration of bone tissue, leading to enhanced fragility and a subsequent increase in the frequency of occurrence of hip and vertebral fractures.

Much still remains to be learned about the aetiology of the disease, about differences in incidence and severity between population groups living in different countries, as well as how to prevent the disease and optimize diagnosis and therapy when it occurs. Although it is generally agreed that osteoporosis is a multifactorial disease, there is little doubt that nutrition is one of the most important of the factors that needs to be taken into account. Included in the many components of the diet that may be important are a variety of minor elements (e.g. calcium, magnesium and sodium) and trace elements (e.g. cadmium, copper, manganese and zinc). Nuclear analytical techniques such as NAA are particularly suitable for the determination of these elements in foods, diets and human tissues, including bone.

The IAEA has just started a new co-ordinated research programme on this topic. It will focus on determining the age of peak bone mass in each study group, and quantifying differences in bone density as functions of the age and sex of persons in the study groups. It will also quantify differences between the study groups in different countries. Supplementary studies will be conducted using NAA relative to the trace-element nutrition of persons in the respective study groups. ❐

Radiation issues, human health, and nutrition research

In recent years there has been a considerable increase in the perception of risk associated with low-level radiation. Concomitantly, there is now a much higher level of concern about the use of radioisotopes in scientific research, particularly if they are administered to normal healthy subjects (and, of course, most of all, if these subjects happen to be children or pregnant women).

Many radioisotope techniques are *in vitro* techniques, which means that the isotope is used in the laboratory as part of an analytical procedure. None of the isotope is administered to the subject, and therefore, for the subject, there is absolutely no radiation hazard. (The only possible hazard is to the scientist who is doing the analysis. Usually he or she has to be classified as a radiation worker, and is required to follow appropriate procedures to minimize the radiation dose to him/herself and co-workers. The possible hazards are extremely small or non-existent and work of this kind is universally accepted to be standard practice for medical and other types of radiation workers.)

For some kinds of nutritional study, however, the most cost-effective procedure is to administer a radioisotope tracer to a test subject (a volunteer). The radiation doses delivered in these kinds of studies are very small. For example, in a typical *in vivo* study of iron uptake using the iron-55/iron-59 dual isotope technique, the dose to the organs receiving the highest exposure is about 0.4 mSv. This is well within the range of variations in normal annual background exposure to radiation (e.g. resulting from living in different geochemical environments or at different altitudes). Expressed another way, it is less than the dose delivered by a modern conventional diagnostic chest X-ray, or about the same as the *additional* radiation dose that an airline passenger would be exposed to on crossing the Atlantic ten times. Although such doses are well within the WHO international ethical guidelines for biomedical research involving human subjects, it is now widely considered to be good practice to exclude children and pregnant women from studies with radioisotopes.

Particularly for children and pregnant women, the currently preferred technique is to use a stable isotope tracer rather than a radioactive one (e.g. iron-58 instead of iron-59). Although the methodologies involved are generally more difficult and more expensive, the use of stable isotopes is without any radiation hazard to the subject and can therefore be justified to ethical committees even for studies in very small children. The IAEA's programmes are also promoting the use of such techniques.

Nutrition, immunity and low-level radiation. Another issue of particular concern is the effect of radiation on the immune system. Radiation is only one of several factors that may influence the general level of immune status in a population; others include nutrition and toxic environmental chemicals. Most investigations of immune status conducted up to now have only focussed on one factor at a time, generally ignoring the others. In populations exposed to higher-than-normal levels of radiation, it is generally difficult, or impossible, to judge to what extent changes in immune status are associated with the radiation and to what extent they may be associated with other factors. A Joint IAEA/WHO Advisory Group Meeting was convened at the IAEA's headquarters in Vienna in May 1994 to throw more light on some of these issues. In particular, the Group was charged with reviewing what is known about these topics and about current research priorities, and to advise the IAEA on the purpose and scope of future actions that could be organized within the framework of a co-ordinated research programme (CRP). The proposed CRP, which is due to start in 1996, will focus mainly on the effects of low-level radiation on immune status in human populations. The main variables of interest are the level of individual radiation exposure, and the nutritional status. Possible study groups include persons living in areas of high radiation background (e.g. in countries where areas of high radiation background are known to occur naturally, or at high altitudes, or in areas affected by the Chernobyl accident). Other possible groups comprise radiation workers and uranium miners.

Nutrition and radiation protection. For the purposes of radiation protection it is convenient to make calculations of radiation doses to individual organs and to the whole body on the basis of a so-called "Reference Man". This is a conceptualized model of a human being whose organ masses, physiological functions, and other characteristics of importance in radiation protection have been defined in a standardized way. Recently, with the financial assistance of Japan, the IAEA's Division of Nuclear Safety has been conducting a programme whose purpose is to refine the concept of Reference Man by collecting data for a so-called Asian Reference Man. Starting in 1995, this programme is due to be extended by new studies which will focus on nutritional and related aspects. The elements of primary interest include caesium, iodine, strontium, thorium, and uranium. The samples of primary interest include nationally representative specimens of total diets and individual staple foodstuffs. The analyses will be done by nuclear and nuclear-related analytical techniques together with other non-nuclear techniques according to the facilities available in the participating countries.