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International and Public Health Nutrition Group Symposium on 'Can nutrition intervention make a difference?'

Combating micronutrient deficiencies: problems and perspectives

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The title of this symposium, 'Can nutrition intervention make a difference?' raises the question of 'make a difference to what?', and raises the issue of how this difference can be measured and attributed to the intervention. The present paper focuses on the micronutrient interventions in which the United Nations Children's Fund (UNICEF) has been providing assistance for many years. It describes the global agreement on the need for action to tackle micronutrient deficiencies and the efforts made since 1990 to improve the micronutrient status of children in countries where UNICEF has programmes. It summarizes information available from the 161 countries and territories in which UNICEF has programmes of assistance, and concludes with some perspectives on ways in which adequate micronutrient nutrition of children and women in developing countries might be achieved as the next millennium approaches.

Global goals

Two global conferences which took place at the beginning of this decade (World Summit for Children in 1990 and International Conference on Nutrition in 1992) established for the first time specific global goals and targets for reducing micronutrient deficiencies and improving child nutrition (UNICEF, 1991; Food and Agriculture Organization/World Health Organization (WHO), 1992). They helped to form a global political consensus that some specific reductions in micronutrient deficiencies in children not only could be achieved, but that they should be achieved by the end of the decade. These conferences helped to create a climate of opportunity whereby change on a global level became possible. The extent to which change has actually occurred has depended on the commitment of individual governments, agencies and individuals to exploit these opportunities.

The World Summit for Children was held at the United Nations, New York, in September 1990. At that time, it was the largest gathering of heads of state ever to take place. It was a meeting of Government leaders, convened by Governments and facilitated by the United Nations, which reached agreement on the need for concerted action on a number of issues agreed to be critical for the future of the world's children. There were three goals specifically related to improving micronutrient status of children and women: the virtual elimination of I-deficiency disorders (IDD), the virtual elimination of vitamin A deficiency and its consequences (including blindness) and a reduction of Fe-deficiency anaemia (IDA) in women by one-third of 1990 levels (UNICEF, 1991). The term 'virtual elimination' was used to indicate the elimination of the deficiency as a public health problem. These goals had been identified in preparatory meetings on the basis that the deficiencies caused serious problems common to many different countries and that there were relatively simple, low-cost and effective approaches to tackling them.

At the International Conference on Nutrition in Rome, December 1992, the Ministers and 'Plenipotentiaries' representing 159 states and the European Economic Community re-affirmed some of the goals of the World Summit for Children when they pledged to make all efforts to eliminate I and vitamin A deficiencies by the end of this decade (Food and Agriculture Organization/WHO, 1992).

When the micronutrient goals were endorsed by the World Summit for Children in 1990, there was no general agreement on exactly which countries had a problem of public health significance in relation to I or vitamin A deficiency, or on the indicators which could be used for monitoring progress towards the achievement of the goals.

Abbreviations: IDA, iron-deficiency anaemia; IDD, iodine-deficiency disorders; UNICEF, United Nations Children's Fund; WHO, World Health Organization.

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Table 1. Criteria for monitoring progress towards eliminating iodine-deficiency disorders as a public health problem

Indicator	Goal
1. Salt iodization	
Proportion of households consuming effectively iodized salt	>90%
2. Urinary I	
Proportion below 100 μg/l	<50%
Proportion below 50 μg/l	<20%
3. Thyroid size	
In schoolchildren 6–12 years of age:	
Proportion with enlarged thyroid, by palpation or ultrasound	<5%
4. Neonatal TSH	
Proportion with levels >5 mU/l whole blood	<3%

TSH, thyroid-stimulating hormone.

WHO and UNICEF organized a series of consultations with groups of scientists to establish a consensus on indicators and methodologies for assessment that could be recommended to countries. The criteria for monitoring IDD elimination programmes are shown in Table 1. Criteria for identifying and monitoring changes in prevalence of vitamin A deficiency included prevalence of night-blindness, four biochemical indicators and conjunctival impression cytology. Most countries have found it practical to determine only serum retinol concentration in large population-based surveys. Serious 'biochemical' vitamin A deficiency was agreed to exist if the prevalence of serum retinol levels $\leq 0{\cdot}70$ μmol/l exceeded 20%, and moderate deficiency to exist if the prevalence of retinol levels below this value was between 10 and 20%. WHO/UNICEF (1993, 1995) also supported work to bring together existing knowledge on the prevalence of I and vitamin A deficiency and tabulated this information according to the newly-established criteria on indicators. WHO (1992) published a report on the global prevalence of IDA in women.

In 1991 and 1992 UNICEF in consultation with Governments and WHO identified a number of the goals of the World Summit for Children for which it appeared particularly rapid progress could be made. Process-oriented targets, known as the Mid-Decade Goals, to be achieved by the end of 1995 were proposed, and specific strategies were suggested in relation to the goals of eliminating IDD and vitamin A deficiency (WHO/UNICEF, 1996). UNICEF, in close partnership with WHO and with significant help and encouragement from bilateral donor agencies and international non-governmental agencies, made particular efforts to help countries take action to achieve these two specific micronutrient goals. Governments and national institutions were provided with assistance to determine the extent and magnitude of the problem of vitamin A and I deficiency where this was not already known. This often involved the provision of training, assistance in establishing laboratory capacity to measure the recommended indicators, support for field work and for the analysis, publication and dissemination of the results. Where I deficiency was identified to be a problem of public health magnitude, countries were encouraged to consider universal salt iodization as the approach of choice. Where clinical vitamin A deficiency occurred as a public health problem, countries were encouraged to establish vitamin A-supplementation programmes, together with other strategies to improve intake of provitamin A carotenoids and retinol.

Progress towards elimination of iodine-deficiency disorders

In a review made by UNICEF of the situation in the 132 developing countries for which information was available, IDD was reported to be a public health problem in 111 countries, to be absent in ten countries and to be of uncertain prevalence in eleven countries.

The iodization of edible salt supplies to combat what is now known as IDD was introduced in Switzerland in 1922 and in the USA in 1924, and proved to be safe and effective in reducing I deficiency. Efforts to combat IDD in the Andean countries of South America through salt iodization in the 1950s and 1960s had also proved effective, although some of these were not sustained. Efforts to combat IDD through salt iodization had also been made in China, India and Vietnam, although attempts to target iodized salt specifically to I-deficient areas in these countries had limited the effectiveness of these programmes. Based on these experiences, and on the growing evidence that marginal levels of I deficiency were far more widely distributed than had been previously thought (Hetzel, 1989), WHO/UNICEF (1996) recommended that all edible salt consumed in a country should be iodized if IDD constituted a public health problem in any part of the country, a strategy that became known as 'universal salt iodization'. The Mid Decade Goal for IDD was agreed to be 'Iodization of all salt for human and animal consumption (including salt used for food processing) in all countries where iodine deficiency disorders are a public health problem' (WHO/UNICEF, 1996).

In 1991, UNICEF estimated that US $100 million would be needed in additional funds, over and above the investment which was expected to come from national governments and local industry, to achieve the Mid-Decade Goal of universal salt iodization. The existence of a clearly identified problem, clear targets and effective strategies to achieve them made support for salt iodization attractive to several development funding agencies. In addition to receiving support from its traditional government donors, UNICEF entered into a partnership with the international non-governmental service organization, Kiwanis International, to raise additional funds to support national IDD control programmes. Table 2 shows the approximate amount and major sources of the nearly US $60 million in development assistance made available to support salt iodization since 1993.

The existence of policies, laws and agreements is one of the most straightforward indicators of progress which can be monitored at the global level. Laws or regulations requiring all edible salt to be iodized now exist in all but seven countries in which UNICEF has programmes and in which IDD is recognized to be a public health problem (Afghanistan, Azerbaijan, Estonia, Haiti, Kyrgyzstan, Latvia and Lithuania have no law or regulation). It is also relatively straightforward to determine the extent of use of

Table 2. External funding resources to support efforts to eliminate iodine-deficiency disorders

Funding agency	Approximate level of funding 1993–mid 1997 (US$ millions)	Countries or purpose
World Bank (loan)	27	China
Canadian International Development Agency, through UNICEF	18	Forty-six countries in Africa and Asia and Peru
Kiwanis International, through UNICEF	6·5	Albania, Bolivia, Central African Republic, Ghana, Guinea, Madagascar, Mexico, Nepal, Philippines, Turkey, Ukraine, Vietnam
USA		Eritrea and Ethiopia + global support for training
Germany		Laos
Japan		Mongolia
Belgium	8	Andean Latin America
Australia		Vietnam, Indonesia
The Netherlands		Training and publications
Total	59·5	

UNICEF, United Nations Children's Fund.

iodized salt by households. The availability of a cheap semi-quantitative test kit has made it possible to include an objective assessment of iodized salt availability in the multi-purpose representative household surveys that UNICEF, WHO and groups such as the US-based Demographic and Health Surveys assist governments to carry out. Questions on iodized salt use have been included in the household surveys recently undertaken in at least fifty countries. Based on these surveys, and on data on the total amount of iodized salt produced or imported, UNICEF estimates that there are now twenty-seven developing countries in which over 90 % of households use iodized salt, and a further fifteen countries in which between 75 and 90 % of households use iodized salt. These countries are shown in Table 3. Forty-eight developing countries with IDD had no significant salt iodization programmes in 1994. Most of these countries have now started to iodize locally-produced salt or to import iodized salt and fourteen of these countries have now iodized more than half their salt. Of the ten countries for which no firm data are available, several are known to be planning to start salt iodization in the near future. Indonesia, Iran, Lebanon, Tunisia and Zambia are examples of countries in which household use of iodized salt has increased substantially in the last 3 years (UNICEF, 1997).

Nepal is an example of a country where IDD has long been known to be highly endemic but where rapid progress in increasing I intakes of vulnerable groups is now being made. Previous approaches to combating I deficiency relied on the provision of high-dose injectable or oral iodized-oil supplements, but this proved to be extremely expensive and there was little prospect that the intervention could be sustained. Since 1993, concerted efforts to promote both the supply of iodized salt and to increase consumer demand have been highly successful. The results of the 1996 Nepal Family Health Survey are shown in Table 4 (Ministry of Health, His Majesty's Government, Nepal 1997). Of a representative sample of households in Nepal in 1996, 93 % were using iodized salt and, reassuringly, iodized salt use differed little by location of household, or educational status of the household head.

In India, iodized-salt production has recently increased by 30 % and it is estimated that 65 % of all edible salt produced for sale is now iodized. A district-level monitor-

Table 3. Percentage of households consuming iodized salt (as of December 1996)

Region	Countries in which 90 % or more of households use iodized salt	Countries in which between 75 and 90 % of households use iodized salt
Latin America	Argentina, Belize, Bolivia, Brazil, British Virgin Isl., Chile, Colombia, Costa Rica, Ecuador, El Salvador, Jamaica, Nicaragua, Panama, Peru	Mexico, Honduras, Paraguay
North Africa, Middle East	Algeria, Lebanon, Libya, Tunisia	Iran, Jordan
Africa	Kenya, Rwanda, Zambia	Burundi, Cameroon, Ethiopia, Eritrea, Namibia, Nigeria, Sierra Leone, Tanzania, Zimbabwe
South Asia	Bhutan, Nepal	
East Asia and Pacific	Laos	Indonesia
Central and Eastern Europe and Newly Independent States	Croatia, Macedonia, Poland	

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Table 4. Percentage of households using iodized salt, by selected background characteristics, Nepal 1996

Background characteristic	Percentage	No. of households
Residence		
Urban	98·6	716
Rural	92·6	7366
Ecological region		
Mountain	89·2	608
Hill	92·2	3695
Terai	94·7	3779
Educational level of household head		
No education	91·9	4806
Primary	94·4	1654
Some secondary	95·7	951
Complete secondary	96·0	560
Don't know or missing	94·6	111
Total	93·2	8082

ing system has been established in twelve northern and central states and, in the nine states for which data are available, over 90 % of households consume only iodized salt compared with the situation in 1992–3 when less than 40 % of salt used by households in these states was iodized. A major past impediment to salt iodization in both India and Nepal has been the popularity among consumers of very large coarse crystals of salt, known as 'bargara'. Although this salt could be iodized it was washed before use to remove dirt, thus removing all the I. Concerted efforts have been made in India to discourage the use of 'bargara' salt through mass campaigns and popular movements, and these have resulted in a marked reduction in the production of this type of salt. The supply of iodized salt in India has increased to meet the increased demand. According to the Salt Department, Ministry of Industry, Government of India, 5·2 million tons of iodized salt were produced for domestic human consumption in 1995 by over 600 manufacturers compared with just 150 thousand tons produced by fifteen manufacturers in 1984 (UNICEF India Country Office, IDD Project (India), unpublished results).

Impact of salt-iodization programmes

A number of countries have been able to conduct representative national or regional assessments of the impact of iodized-salt use on biological indicators of I deficiency. However, the collection of urine samples and the determination of urinary I concentration using the laboratory methods presently available poses considerable problems in many countries. The determination of goitre size by palpation in large surveys with several different assessment teams is also difficult, particularly when goitres become smaller as the result of interventions. The use of portable ultrasound machines for goitre sizing has been recommended, and has been used in surveys in some countries in Latin America and Africa, but the cost of this equipment has limited its use. Bolivia is an example of a country where substantial efforts have been made to monitor both urinary I excretion and goitre size on a national scale since iodized salt was introduced. Large sample surveys carried out in this Andean country in the early 1980s showed that the prevalence of goitre was above 60 % in children at primary school. A national control programme was started in 1983. A 1996 nationally representative survey (Secretaria Nacional de Salud, 1996) found that the median urinary I excretion was 250 μg/l and only 10·2 % of all urine samples had an I concentration of less than 50 μg/l. The median urinary I excretion was found to be above minimum desired levels in samples from all administrative departments of the country and in both rural and urban areas. Iodized salt was used in 92 % of households. On the basis of these and other data, Bolivia was the first country to declare, in September 1996, that it had achieved the goal of 'virtual elimination of IDD'.

UNICEF has estimated, based on global assessment of goitre prevalence made by WHO/UNICEF (1993), that in 1990 about forty million infants globally, one-third of all babies born each year, were at some risk of mental impairment due to I deficiency *in utero* or in early childhood. In 1997, based on the worldwide increase in the use of iodized salt noted previously, it is likely that a substantial proportion, perhaps as many as twelve million, of the infants born this year in areas where the risk of I deficiency was previously high have been protected from that risk. Because overt epidemic cretinism is a relatively rare event, even in severely-I-deficient populations, and because it is now recognized that there is a continuum of mental impairment with progressively inadequate I intakes (Boyages, 1994), it is impossible to estimate with any precision the number of people suffering from clinical cretinism due to I deficiency. Using the limited data available, UNICEF estimated that there were about 100 000 children born each year with cretinism due to I deficiency in 1990. As the proportion of the world's population at risk of I deficiency and consuming iodized salt approaches 60 %, it is likely that the number of new cretins born each year has now also fallen substantially.

Although the global effort to iodize salt has been mainly justified on the basis that deficiency *in utero* and in early childhood irreversibly reduced mental development (Bleichroidt & Born, 1994), other benefits of increased I intake in areas with a high prevalence of IDD may include a reduction in the rates of still-birth, spontaneous abortion and infant mortality (Chaouki & Benmiloud, 1994). A recent study in West Java, Indonesia, found a 72 % reduction in the risk of death during the first 2 months of follow-up in infants who were given a supplement of oral iodized oil at about 6 weeks of age compared with controls given a placebo (Cobra *et al.* 1997). Adequate population-wide I intake will also reduce the risk of irradiation of the thyroid gland by ^{131}I and the resultant thyroid cancer incidence in the event of accidents in nuclear plants (Ermans, 1993).

Problems

Todd *et al.* (1995) in Zimbabwe and Bourdoux *et al.* (1996) in Zaire have reported an increase in thyrotoxicosis in adults and suggested that this was caused by a high I intake occurring as a result of salt iodization. To determine whether inappropriately high amounts of I were being added to salt, and to identify corrective measures if necessary, WHO, UNICEF and the International Council for the Control of IDD, in collaboration with national authorities, organized a multi-centre study of salt I levels and urinary I excretion in seven African countries in 1996. The study found a high level of variability in salt I levels and urinary I excretion levels which were normal or high in all countries. Ensuring relatively constant levels of I in salt is the major problem encountered in salt iodization programmes in developing countries where salt is frequently produced on a relatively small scale by many different producers using rudimentary technology. Based on the results of this study and data suggesting that losses of I during storage of salt iodized with KIO_3 were lower than previously believed, WHO, UNICEF and the International Council for the Control of IDD (WHO, 1996) revised earlier recommendations on salt iodization levels. It is now recommended that the I concentration in salt at the point of production should be within the range of 20–40 mg I/kg salt. Better quality-control procedures in factories producing iodized salt, and more extensive regular monitoring of urinary I excretion levels, with adjustment of salt iodization levels where necessary, were recommended. Efforts are now underway to implement these recommendations.

The major challenge will be to ensure that salt iodization continues in countries in which the prevalence of IDD decreases. There is a danger that as visible goitre disappears, public awareness of the importance of iodized salt will decrease, demand for iodized salt will fall and commercial salt manufacturers will cease to purchase the necessary supplies. Governments will need to establish and maintain strong monitoring systems, and ensure that the benefits of adequate I intakes continue to be well understood, to ensure that this does not happen.

Vitamin A deficiency

A meta-analysis of ten different trials, which was commissioned by the United Nations Sub-Committee on Nutrition determined that there was conclusive evidence that improving vitamin A status of young children in regions where vitamin A deficiency occurred reduced mortality rates by 23 % (Beaton *et al.* 1993). Based on this work it was decided to recommend that priority should be given to reducing the prevalence of vitamin A deficiency in younger children. The Mid-Decade Goal for reduction of vitamin A deficiency was agreed to be 'Ensure that at least 80 % of all children under 24 months of age living in areas with inadequate vitamin A intake receive adequate vitamin A through a combination of breast-feeding, dietary improvement, fortification and supplementation' (WHO/UNICEF, 1996).

Magnitude of the problem

Based on the review by WHO/UNICEF (1995) and recent updates from UNICEF field offices, clinical vitamin A deficiency in children is reported to exist in thirty-eight countries, and subclinical deficiency in forty countries. Forty-two countries are unsure whether a problem of vitamin A deficiency exists or not. Vitamin A deficiency in children is reported to exist, or to be likely to exist, in most countries in Africa and South Asia. Representative sample surveys, either national or regional, to determine serum retinol concentration in young children have been made in forty-two countries since 1987. Fig. 1 summarizes the results of the twenty-five national surveys for which reports are available, with data added from USA (Second National Health and Nutrition Examination Survey; Life Sciences Research Office of Federation of American Societies for Experimental Biology, 1985) and UK (National Diet and Nutrition Survey; Gregory *et al.* 1995) surveys for

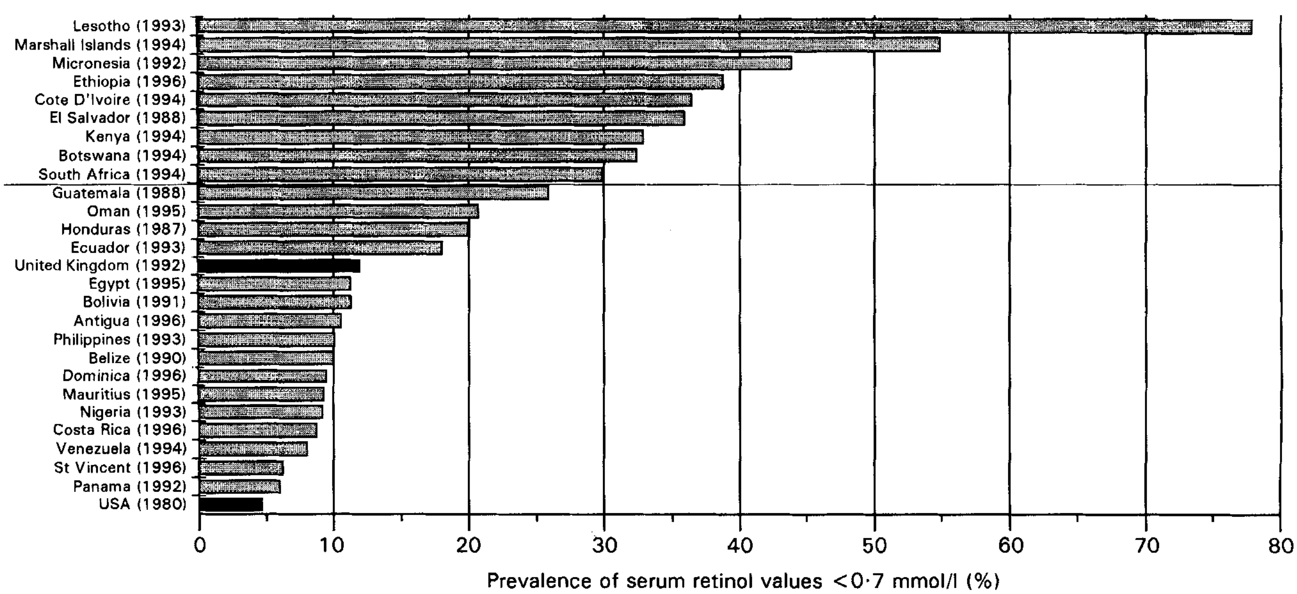

Fig. 1. Prevalence of low serum retinol levels in countries in which nationally representative surveys have been undertaken since 1980. (Data for USA from Life Sciences Research Office of Federation of American Societies for Experimental Biology (1985) and for UK from Gregory *et al.* 1995.)

comparison. Seventeen countries plan to undertake an assessment, or re-assessment, of children's vitamin A status in the near future.

Progress in reducing vitamin A deficiency

Recent information on national policy regarding vitamin A supplementation of children is available for sixty-one of the seventy-eight countries in which vitamin A deficiency exists as a public health problem. All thirty-five countries where clinical deficiency exists, with the exception of Sri Lanka, Angola, and Yemen, and all but fourteen of the twenty-six countries where subclinical deficiency exists (China, Argentina, Colombia, Costa Rica, Dominican Republic, Peru, Namibia, Antigua and Barbuda, Dominica, St Vincent and Grenadines, Central African Republic, Guinea-Bissau and Mauritius) have adopted a policy of routine supplementation of children with periodic high-dose supplements. The majority of countries implementing vitamin A supplementation programmes have adopted the policy recommended by WHO/UNICEF/International Vitamin A Consultative Group (1997) which calls for children aged 6–12 months to receive 30 mg retinol once every 4–6 months and for children aged 12 months and over to receive 60 mg retinol once every 4–6 months. Fifteen countries use alternative supplementation regimens in which a lower dose of vitamin A is provided.

At least thirty-four countries now routinely provide vitamin A supplements together with immunizations during annual 'National Immunization Days'. The National Immunization Days typically take place only once each year, but several countries including Myanmar and Bangladesh have organized additional periods, half-way between the annual immunization days, when high-dose vitamin A supplements are distributed. In other countries, high-dose vitamin A supplements are provided during routine Mother and Child Health clinic visits, often linked to the provision of child immunizations or through community-organized nutrition-improvement programmes. In at least three countries (Mauritania, Marshall Islands, and the Federated States of Micronesia), vitamin A supplements are given twice per year together with antihelminthics to all children.

Fig. 2 shows the percentage of under 5-year-old children in countries which have a national vitamin A supplementation policy that have received high-dose vitamin A supplements during 1994 and 1996 (based on data available to UNICEF country offices from routine service reports or from multi-purpose household surveys). Of all young children in developing countries (with a vitamin A supplementation policy), 50 % received high-dose vitamin A supplements in 1996 compared with 31 % in 1994.

Countries in which the UNICEF office has recently reported that at least 80 % of children under 5 years of age routinely receive high-dose vitamin A supplements include Bangladesh, Bhutan, Bolivia, Cambodia, Federated States of Micronesia, Honduras, Laos, Marshall Islands, Mauritania, Myanmar, Oman, Philippines, Thailand, Vietnam, Yemen and Zambia. Between 50 and 80 % of children under 5 years of age are reported to have recently received high-dose vitamin A supplements in Afghanistan, Angola, Cameroon, Ecuador, El Salvador, India, Indonesia, Iraq, Madagascar, Malawi, Nepal, Nicaragua, Nigeria, Panama, Romania, Sudan and Togo.

Most countries which support the use of high-dose vitamin A supplements procure their supplements through UNICEF's Supply Division located in Copenhagen. Consolidated purchasing on behalf of multiple countries results in low costs. A single 60 mg retinol gel capsule from UNICEF Copenhagen currently costs US $0·02.

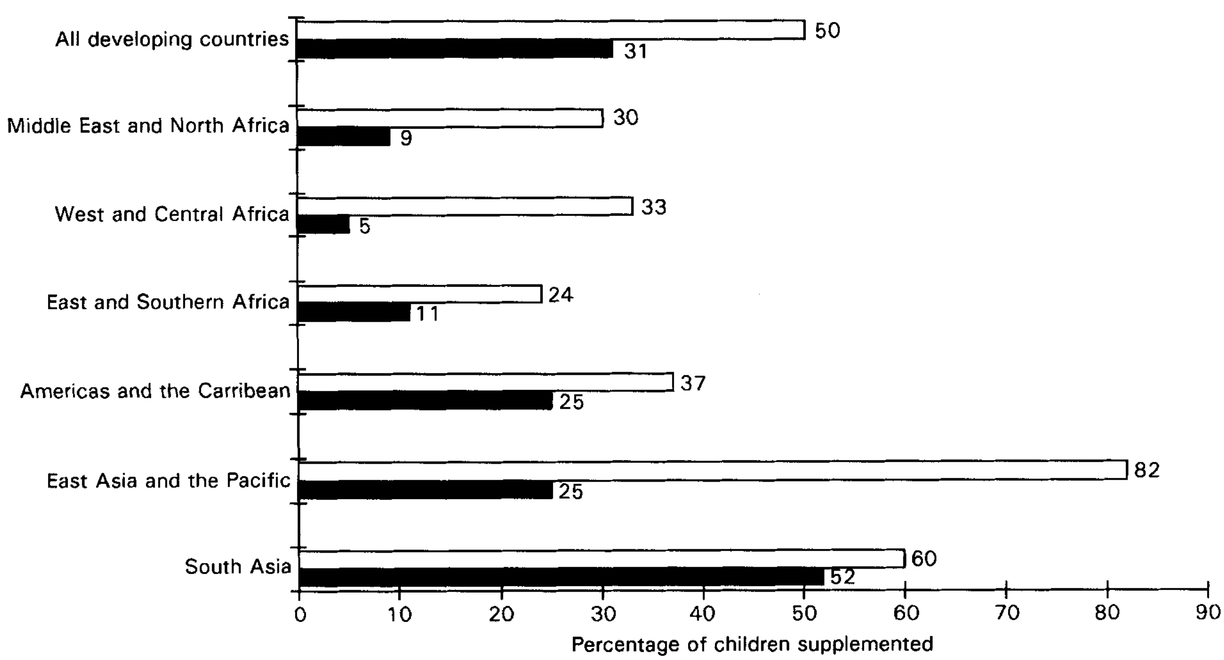

Fig. 2. Children under 5 years of age receiving high-dose vitamin A supplements in 1994 (■) and 1996 (□).

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Table 5. Countries in which more than 10 % of mothers receive high-dose vitamin A supplement postpartum

Country	Percentage of mothers receiving high-dose vitamin A supplements postpartum
Nigeria	90
Bhutan	80
Iraq	64
Indonesia	57
Honduras	53
Vietnam	53
Federated States of Micronesia	50
Malawi	39
Burkina Faso	30
Bolivia	26
Ethiopia	15

Four hundred and sixty million such capsules were supplied during the period 1993–6 at a total cost of US $9·2 million.

WHO/UNICEF/International Vitamin A Consultative Group (1997) recommend that in countries where vitamin A deficiency is a problem, all mothers should receive a high-dose supplement of 60 mg within 8 weeks of delivery. Supplements to lactating mothers have been shown to maintain adequate breast-milk concentrations of vitamin A for up to 6 months (Stolzfus *et al.* 1993). Forty-six countries have established a policy of routinely providing high-dose supplements to all women postpartum. Table 5 lists countries in which more than 10 % of mothers were supplemented, according to the most-recently-available data.

Sugar has been fortified on a national scale in Guatemala since 1974 and there is evidence that this programme has reduced vitamin A deficiency significantly in preschool children (Arroyave, 1986). Honduras and El Salvador introduced sugar-fortification programmes in 1976. Vitamin A-fortified sugar has also been marketed in limited areas of Bolivia and Brazil, and production has recently started in the Philippines. Plans are being developed to fortify sugar with vitamin A in Zambia and Uganda, and in India there is interest in fortifying the sugar which is distributed at a subsidized price to low-income families through the public distribution system.

Impact

There have been few attempts to determine the impact of large-scale routine vitamin A supplementation programmes on survival, health or growth. UNICEF is supporting work in a number of countries which, it is hoped, will be able to relate changes in young-child mortality to improvements in vitamin A status.

Problems

Where a high proportion of children attend Mother and Child Health Centres for other preventative services such as immunization, the additional cost of providing a high-dose vitamin A supplement is small, and high coverage rates are possible. However, in many of the poorest areas of the world where vitamin A deficiency is most common, access to health facilities may be very limited. The recent popularity of National Immunization Days has provided an opportunity to provide vitamin A supplements at the same time as vaccine. However, National Immunization Days are organized primarily to eradicate poliomyelitis, and it is unlikely that they will continue beyond the year 2000 in most regions. It will be necessary, therefore, for vitamin A supplementation to be integrated into ongoing routine child immunization programmes, or for other ways to be considered of ensuring that children receive supplements regularly. The distribution of low-dose vitamin A supplements that could be provided on a weekly or monthly basis in community-organized and -managed programmes deserves consideration.

Iron-deficiency anaemia

WHO (1992) reported that in 1988 56 % of women in developing countries had haemoglobin levels below 110 g/l. The prevalence was reported to be highest in South Asia where 75 % of pregnant women had low haemoglobin levels. Despite being the most prevalent micronutrient deficiency, the World Summit for Children in 1990 established only the modest goal of reducing levels of anaemia by one-third of 1990 levels. No Mid Decade Goal for the reduction of IDA in women or children was established. There is less global consensus on indicators for monitoring progress, or even on optimum supplementation strategies for pregnant women, and no authoritative and up-to-date guidelines for international use on these subjects have been published.

No global data on the prevalence of IDA in young children have been compiled, and no global goal for reduction of IDA in children was defined. Awareness of the importance of IDA in young children is growing, particularly because of the strong associations between IDA and impaired mental and motor development among infants and young children, and poor school achievement in older children (Draper, 1997).

Iron supplements for pregnant women

As with vitamin A, UNICEF is a major supplier of Fe–folate supplements for use by pregnant women in developing countries. During the years 1993–6 a total of 2·7 million packs of 1000 tablets, each containing 200 mg $FeSO_4$ and 0·25 mg folic acid, were shipped to 122 countries at a total cost of US $7·5 million. The average annual supply of Fe supplements from UNICEF alone has been sufficient to ensure that over 50 % of pregnant women would have received at least one tablet each day during the second two trimesters of pregnancy in a few countries, such as Malawi and Bhutan. In many other countries, however, the Fe supplements provided by UNICEF meet less than one-third of the supplements which would be required if national policies of providing supplements to all pregnant women were fully implemented. Information on other sources of supply of Fe supplements in countries where

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UNICEF has programmes has not been compiled, but it is likely that an inadequate supply of supplements is one of the factors limiting the effectiveness of present programmes (Yip, 1996). Other factors limiting programme effectiveness described by Yip (1996) are access to the primary health care system, quality of counselling about need for Fe supplementation and side-effects, and compliance.

Most national programmes of preventative Fe supplementation in pregnancy provide daily supplements of either 200 or 400 mg $FeSO_4$ during the last two trimesters of pregnancy. Based on a number of recent studies suggesting weekly Fe supplements may be as effective as daily supplements (Ridwan *et al.* 1996), weekly supplement regimens for pregnant women have been introduced in Ecuador and Morocco. In the Central Asian Republic and Kazakhstan region, a plan is being developed to reduce IDA through a combined programme of Fe fortification of wheat flour and the use of weekly Fe supplements before pregnancy and during pregnancy.

Iron fortification

UNICEF, WHO and other international partners are supporting the fortification of staple foods with Fe in countries where this would be likely to increase the Fe intake of vulnerable population groups. There is extensive experience with Fe fortification of wheat flour in industrialized countries such as the USA and the UK, although the impact of these programmes has not been well documented (Clydesdale & Wiemer, 1985). Latin America and the Middle East are two regions of the world where wheat flour is widely consumed by all population groups, and where most wheat flour is milled in a small number of relatively sophisticated mills; two factors which make Fe fortification of flour an attractive intervention to help reduce IDA in women and children. The Government of Venezuela enacted legislation in 1993 which required that all wheat and maize flour be fortified with Fe and B vitamins. A 1996 evaluation concluded that this had reduced the prevalence of anaemia in children between the ages of 7 and 15 years at a time of general economic decline (Layrisse *et al.* 1996). Wheat flour is also required to be fortified with Fe in Chile, Guatemala and Trinidad and Tobago. Colombia and Bolivia plan to introduce legislation requiring wheat flour to be fortified with Fe in 1997. Mexico, Ecuador, Paraguay and Brazil are also considering requiring Fe fortification in maize and/or wheat flour.

At a meeting hosted by the Government of Oman in Muscat in October 1996, representatives of the government and the wheat milling industry from eleven countries in the Middle East and North Africa agreed that the fortification of wheat flour with Fe should be introduced as soon as possible as a measure to help reduce the high prevalence of IDA in the region. Wheat is the main staple food consumed in all countries in the region. All wheat flour is already fortified with Fe in Saudi Arabia, pilot fortification in limited areas is underway in Egypt and Iran, legislation on fortification has been drafted in Oman, and national committees or multi-sectoral task forces to develop Fe fortification have been established in Bahrain, Kuwait, Jordan, Lebanon, Morocco, Syria and Tunisia.

Other micronutrient deficiencies

Whilst establishing no specific goals, the Plan of Action for Nutrition adopted by the International Conference on Nutrition in 1992 (Food and Agriculture Organization/WHO, 1992) noted that deficiencies of other micronutrients such as folate and other B-complex vitamins, vitamin C, Se, Zn and Ca also significantly affect health and may merit increased attention by governments.

The evidence that Zn deficiency may significantly impair the immune response of young children in many developing countries and that Zn supplements may both prevent and reduce the severity of common diseases such as diarrhoea and lower respiratory tract infection now appears quite strong (Child Health Research Project, 1997). The difficulties in assessing Zn status may mean that it will not be possible to target interventions to improve Zn status to high-risk areas. UNICEF agrees with Hambridge (1997) that special attention should be given to research that facilitates the design of effective community-based strategies to prevent Zn deficiency. UNICEF and WHO are supporting a series of studies in Indonesia, Vietnam and Bangladesh to demonstrate the effect on growth, prevalence of diarrhoeal disease and anaemia of a combined oral supplement of 12·5 mg Fe and 5 mg Zn provided to infants at 6 months of age for 6 months.

Knowledge of the prevalence of vitamin D deficiency and its importance in countries where UNICEF has programmes is limited. UNICEF supports the use of vitamin D supplements in Mongolia, where 80 % of children under 3 years of age were reported to have been provided with supplements in 1996. Combined low-dose vitamin A and vitamin D supplements are now being provided by UNICEF to children in the Democratic People's Republic of Korea. A general lack of awareness of the potential existence of vitamin D deficiency and its consequences results in little significant action being taken at the present time. UNICEF has recently established new or expanded programmes of cooperation in several countries north of latitude 30°, which includes much of China, Kazakhstan, Uzbekistan, Turkmenistan, Kyrgzstan, Azerbaijan, Iran, Ukraine and Romania. In these regions subclinical vitamin D deficiency may be common, particularly during the winter months. The prevalence of rickets in China in 7-year-old children is reported to be approximately 20 % in the country as a whole and rates in the rural north are as high as 50 % (Hesketh & Xing Zhu, 1997). More surprisingly, 41 % of children attending as outpatients in Ethiopia were recently reported to have clinical signs of rickets, and rickets was found to be associated with an increased risk of pneumonia (Muhe *et al.* 1997). UNICEF is working to increase awareness of the potential problem of vitamin D deficiency and is developing approaches to tackle the problem which will include advocating adequate exposure to the sun as part of better child care practices, and the use of combined low-dose vitamin A and vitamin D supplements where these appear necessary. In the support of the use of combined low-dose vitamin A and D supplements, UNICEF has come full circle, since one of the first nutrition interventions supported by the agency was the provision of $5 million worth of cod-liver-oil capsules for distribution to children in Austria, Czechoslovakia, France, Greece, Italy and Poland in 1951.

Future perspectives

Monitoring and assessment

The availability of cheap, non-invasive and reliable field techniques for determining urinary I content, or marginal vitamin A status (perhaps using dark adaptometry; Congdon *et al.* 1995) would greatly facilitate the establishment of sustainable systems to monitor progress towards eliminating vitamin A and I deficiency in developing countries. Rapid methods of assessing the vitamin A and Fe contents of fortified foods, and more reliable semi-qualitative methods of determining the I content of fortified salt would also be extremely useful.

Micronutrients and pregnancy

Among goals of the World Summit for Children in 1990 were the reduction in the maternal mortality rate by half and reduction in the rate of low birth weight to less than 10 %. Little progress has been made in these areas. About 20 % of babies born in developing countries and over 30 % of babies born in South Asia weigh less than 2·5 kg (UNICEF, 1997). It has been postulated that the markedly higher prevalence of underweight children in South Asia (50 %) compared with Africa (30 %) is partly due to the high prevalence of low birth weight in South Asia (UNICEF, 1996). Maternal mortality rates are between thirty and 100 times higher in Africa and South Asia than they are in Western Europe (UNICEF, 1996).

Few specific actions have been supported in developing countries to reduce the prevalence of low birth weight. Although UNICEF does support a range of activities to improve the overall status of women, including pregnant women, and supports the development of antenatal services, including nutrition education, the impact of these actions on prevalence of low birth weight is rarely monitored. The lack of specific actions reflects the lack of any scientific consensus on the nature of effective interventions. Gulmezoglu *et al.* (1997) have reviewed 126 randomized controlled trials of thirty-six prenatal interventions to prevent or treat impaired fetal growth and found that only smoking cessation, anti-malarial chemoprophylaxis in primigravidae and balanced protein–energy supplementation were likely to be beneficial, but concluded that Zn, folate and Mg supplementation in gestation merited further research. It is striking that the majority of well-conducted clinical trials of micronutrient supplementation in pregnancy have been done in rich countries, where diets are rarely grossly deficient in any particular micronutrient, and where the prevalence of low birth weight and poor pregnancy outcome is low. Further support for good trials in regions of the world where the problems are most severe would be of significant help in developing feasible interventions.

There is considerable evidence that vitamin A deficiency impairs immunity in children, making infections more severe and more likely to be life-threatening (Sommer & West, 1996). Of the maternal deaths in developing countries, 11 % are directly attributed to infections (UNICEF, 1996). Night-blindness in pregnancy in women in developing countries seems to be far more common than has been recognized previously, and it appears plausible that vitamin A deficiency in pregnancy may be one factor contributing to high maternal mortality rates. A large-scale randomized controlled trial to investigate the impact of weekly supplements of β-carotene or retinol on pregnancy outcome is currently underway in Nepal. If the results of this survey show a reduction in maternal morbidity or mortality, developing countries with high maternal mortality rates will need to consider how they might increase vitamin A or β-carotene intakes of pregnant women. WHO and the Micronutrient Initiative (1997) have recommended that where vitamin A deficiency is endemic among preschool-age children and maternal diets are low in vitamin A, health benefits are expected for the mother and her developing fetus with little risk of detriment to either from either a daily supplement not exceeding 3000 μg retinol anytime during gestation, or a weekly supplement not exceeding 8500 μg retinol.

A combined vitamin–mineral supplement for pregnant women in developing countries is an option that needs to be considered. Such a supplement might contain Fe, folic acid, Zn and vitamin A, together perhaps with riboflavin, Ca and Mg. Such supplements are widely used in industrialized countries, although there is no consensus on their effectiveness and no national or international guideline on their composition. In such a supplement, interaction between different components which reduces the bioavailability of some micronutrients may be a significant problem and further research in this area is required. The retail cost of 'generic' multi-vitamin–mineral prenatal supplements available in the USA, which claim to provide approximately 100 % of the US 'daily value' of vitamin A, Zn, vitamin D, and folate, together with 60 mg elemental Fe, is presently about eleven times higher than the price at which UNICEF supplies Fe–folate supplements containing the same amount of Fe. It is possible, however, that this price might be reduced through bulk purchasing and local manufacture to a level that would make the widespread use of such supplements feasible in developing countries. Weekly doses of vitamin A and vitamin D would be likely to be both safe and effective, and if a consensus is reached that weekly doses of Fe are also effective, a weekly multi-micronutrient supplement may be a possibility. No data on the effectiveness or safety of weekly doses of either folate or Zn appear to exist.

There is a broad consensus that adequate folic acid intake periconceptionally can reduce neural-tube birth defects. Cereal flours will be required to be enriched with folic acid in the USA from 1 January 1998 in order to prevent neural-tube defects. There is very little information on the prevalence of neural-tube defects in developing countries, but the little there is suggests that the prevalence in countries such as Mexico and South Africa may be several times higher than it is in the USA or Western Europe (International Clearing-house for Birth Defects Monitoring Systems, 1996). Folic acid fortification of wheat flour or other staples can be introduced at very low cost in countries that are already adding Fe. Oman, Colombia and Bolivia are considering this option.

Fortification

In the last few years it has been proved possible to fortify a considerable proportion of the salt consumed in the world with I. Unfortunately, there are few other food vehicles which are centrally processed and widely consumed in poor countries in approximately constant amounts. The poorest people in the poorest countries are disproportionately affected by micronutrient deficiencies and they eat little processed food. Processed foods which are consumed, in decreasing order of importance, are salt, sugar and vegetable oil or oil products. In many countries in Latin America the cereal staple is now centrally processed, making fortification with Fe, folate, vitamin A and other micronutrients feasible and likely to be effective. In many countries in Africa and Asia, however, the staple cereal is processed either at home or in a small village facility in which fortification is likely to be extremely difficult. Sugar fortification with vitamin A, or possibly with Fe, remains a possibility which could be further exploited. Fe can also be added to household salt together with I, and a large-scale trial of Fe–I-fortified salt is currently underway in Ghana. Using present technologies, however, the quality of salt required and the sophistication of salt processing for the production of Fe–I-fortified salt will be beyond the capacity of many developing countries.

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