**Introduction**

Micronutrients are those vitamins and minerals needed—but not manufactured—by the body in small amounts for a wide range of functions and processes that are crucial to optimal human growth, development, and healthy maintenance of the body over a life span. Micronutrient deficiencies can cause learning disabilities, mental retardation, decreased immunity, low work capacity, blindness, and premature death. The most common micronutrient deficiency conditions result from inadequate amounts of iodine, iron, and vitamin A in the body. Fortunately, the technology for preventing and controlling micronutrient deficiencies is relatively simple and cost-effective to implement, making it possible for countries to improve the health, well-being, and productivity of their populations in a fairly short time frame.

**General intervention strategies**

Combinations of three main strategies—increased dietary intake of micronutrients, fortification of common foods with micronutrients, and direct supplementation of high-risk groups—are the most frequent approaches used to prevent micronutrient deficiency diseases.

Particularly for vitamin A, changes in behavior (for example, increasing children’s intake of orange fruits such as mango and papaya), can achieve significant improvements in micronutrient status at little or no increased cost to households. Relying on improved dietary diversity and increased micronutrient intake from food is the most sustainable solution, but sometimes it is not possible to fully meet micronutrient requirements through the available diet (iodine in particular and frequently iron). Developed countries have successfully implemented universal fortification programs to eliminate or reduce substantially, vitamin A deficiency (VAD), iodine deficiency disorders (IDD), and iron deficiency anemia (IDA).

There are many advantages to food fortification: It is generally more cost effective than supplementation, offers an intervention that makes sense...
for the long-term, reaches (ideally) all segments of a population, and does not require individual compliance or substantial behavior modification to achieve improved micronutrient status. There are however, a number of conditions that must be met in order to successfully implement universal fortification of foods with micronutrients (see Annex C, Box C-1).¹

Supplementing targeted at-risk groups (or in areas of high deficiency prevalence, the entire population) with micronutrients may be an important strategy to consider. Because many supplementation programs are delivered through existing health care systems, there are often problems with adequate coverage, supply and delivery system obstacles, and program sustainability. However, micronutrient supplements are relatively low in cost and highly effective in their ability to correct micronutrient deficiencies if program implementation constraints can be overcome.

**Vitamin A**

*Functional importance*

Vitamin A is vital to human health for a number of reasons. It is: i) essential to the health of the eye and the ability to see in low light, ii) necessary for protein synthesis which affects growth, iii) critical to the body’s immune system, and iv) appears to play a protective role against the development of certain types of cancer.

*Sources of vitamin A*

There are two forms of vitamin A found in food: retinol or preformed vitamin A and carotene. Retinol or preformed vitamin A is obtainable only in animal

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¹. For detailed information about fortifying food with micronutrients, refer to the 1996 publication *Micronutrient Fortification of Foods: Current Practices, Research and Opportunities* by M. Lotfi, et al. It is available from the Micronutrient Initiative by e-mailing mi@micronutrient.org. Web: www.micronutrient.org.
products (e.g., liver, kidney, small whole fish, butter, egg yolk, breastmilk, whole cow’s milk, cheese made with whole cow’s milk, fortified skim cow’s milk) and is more effective than carotene in increasing the body’s vitamin A stores (among several types of carotene, \( \beta \)-carotene is the most important). Carotene is plant-based, and present in yellow, orange, and green fruits and vegetables (e.g., collard greens, spinach, carrots, sweet potatoes, mango, squash, apricots, red palm oil). Recent evidence suggests that the carotene in fruits is used more efficiently than that in vegetables (International Vitamin A Consultative Group [IVACG], 1996).\(^2\)

### Absorption and storage of vitamin A

Fat, protein, zinc, and vitamin E assist the body in the absorption of vitamin A, and fat in particular, is needed in the diet for maximum absorption. Because vitamin A is fat soluble, the body is able to store up to 6 months supply of vitamin A in the liver. In a process similar to iron metabolism, it appears that the body regulates the absorption of vitamin A to avoid an overload by decreasing absorptive efficiency as vitamin A status improves.

### Measurement of vitamin A

Vitamin A and carotenoids can be quantified in several different units, but it is preferable to use the International System of Units (SI) such as \( \mu \text{mol} \). See Box 3-1. Another way to measure vitamin A uses Retinol Activity Equivalents, or RAEs. These were introduced by the U.S. Institute of Medicine to replace retinol equivalents. They reflect differing bioefficacy of various carotenoids.

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\(^2\)The apparent differential in bioavailability of carotenoids in fruits and vegetables has been tentatively explained by: the tendency of provitamin A to be trapped in the fibrous cells of vegetables; certain preparation methods (grinding or pureeing foods usually increases bioavailability of provitamin A, while cooking and drying in the sun can cause vitamin A activity to be lost); and, the composition of the meal in which provitamin A food is consumed (International Vitamin A Consultative Group, 1996).
Vitamin A deficiency

Vitamin A deficiency (VAD), a public health problem found in at least 75 countries, affects more than 200 million children at some level. It is the leading cause of preventable blindness, causing as many as 500,000 preschool children to go blind each year. In addition to ocular effects, VAD is associated with increased mortality (up to an additional 1 million children...
die from infections they would otherwise survive had they been vitamin A-replete) and severity of morbidity from respiratory and gastrointestinal diseases because of the role vitamin A plays in the human immune system. Several studies have shown more rapid progression from HIV to AIDS and increased mortality in vitamin A-deficient adults (International Vitamin A Consultative Group [IVACG] 2000).

VAD is most common among young children because of their higher (relative to other ages in a life span) nutrient needs to support rapid growth and the high incidence of infections characteristic of this age group. Illness reduces appetite that, in turn, reduces intake of vitamin A-rich (and all other) foods. Bacterial and parasitic infections of the gut reduce vitamin A absorption, and many infections including diarrhea and measles actually increase the body’s requirements for vitamin A. Pregnant and lactating women are another high-risk group for VAD. Recent research (International Vitamin A Consultative Group, 2002) suggests that maternal night blindness may be a good marker for detecting households and communities of children at risk for VAD and it is a clear indicator for infants at risk of vitamin A-deficient breastmilk consumption. Prevalence of night blindness in pregnant women of more than 5% suggests that there is a public health problem with increased risk of anemia, protein energy malnutrition and maternal and infant mortality.

Assessing vitamin A deficiency as a public health problem

Traditionally, identification of VAD in populations relied on clinical signs and symptoms of xerophthalmia (a range of disorders affecting the eye, beginning with nightblindness and progressing to corneal damage and eventual blindness). Recent studies now suggest that the presence of clinical signs and symptoms of the deficiency indicates that depletion of vitamin A is well beyond the point for determining that a public health problem exists. Subclinical deficiency can be identified through biochemical analyses of blood samples. However, no biochemical indicators for use under field survey conditions are both adequately sensitive and
specific to be used alone. Therefore, combinations of indicators and risk factors have been identified to determine when a public health problem is present. Table C-1 and Table C-1a in Annex C contain the WHO guidelines for assessment of VAD as a public health problem.

**Assessment methodologies and indicators**

**Serum retinol** is the biochemical indicator of vitamin A status most commonly used in studies of VAD\(^3\) although it is not reliable in people with concurrent or recent infections (serum retinol levels drop). Experiments with analytical procedures show promise of simplifying blood sample analysis under field conditions and thereby improving the feasibility of using serum retinol as a stand-alone population-based assessment tool in the near future. Serum retinol levels of \( \leq 0.70 \, \mu\text{mol/L} \) (or \(< 20 \, \mu\text{g/dL} \)) are considered indicative of mild-moderate deficiency for children 6–71 months of age (WHO/UNICEF, 1994).

Dietary analysis continues to be a standard assessment method but it is important to note that this methodology assesses risk—not the actual condition—of vitamin A status. Helen Keller International (HKI) found that a semiquantitative food frequency questionnaire (FFQ) used in rural India was successfully able to identify areas where VAD was likely to be a problem as well as suggest possible intervention strategies. It should be noted that FFQs commonly overestimate the amount of vitamin A consumed in the diet when compared to weighed food intake. One suggestion is to use a population mean 24-hour intake to get closer to the true average daily intake.

\(^3\) Other indicators of subclinical vitamin A status include conjunctival impression cytology (CIC), impression cytology with transfer (ICT), relative dose responses (RDR) and modified relative dose response (MRDR) measurements, and breastmilk vitamin A.
A variety of ethnographic research methods have been usefully employed in planning for successful vitamin A intervention projects (International Vitamin A Consultative Group meeting proceedings [IVACG], 1996). One example of a focused ethnographic protocol for community-based collection of information about vitamin A used food system data tables, food frequency questionnaires and 24-hour recalls, a market survey, key informant interviews, belief and behavior mapping, structured interviews to elicit data on food availability, vitamin A contents of food, amounts eaten, reasons for eating, and the beliefs and behaviors specific to clinical VAD. This particular protocol took 6–8 weeks to implement. Findings generated by the studies included the importance of seasonality of vitamin A-rich foods, local food beliefs and taste preferences, ecological and socioeconomic constraints to consumption of vitamin A-rich foods, perceptions of clinical VAD, and the local responses to signs and symptoms of the deficiency.

**Preliminary case finding**

The World Health Organization (Sommer, 1995) recommends a preliminary case-finding exercise when determining whether or not vitamin A deficiency exists in a particular area. A specialist experienced in identifying active or healed cases of xerophthalmia will conduct interviews with local public health officials, clinicians, nutritionists, and community health workers about the presence of the problem. He/she will review medical charts of children in clinics, hospitals, and schools for the blind, and search for clinically active cases among high-risk children (e.g., children attending feeding centers, clinics, those admitted to hospital wards, and those living in urban slums or impoverished rural communities). Documenting old cases of healed xerophthalmic disease and collecting data on dietary intake and serum retinol levels are part of this first step in assessing VAD in a population. When there is evidence that VAD does or may exist, a definitive assessment of the magnitude and distribution of the condition should be undertaken.
Definitive assessment

To quantify the extent of VAD, a population-based prevalence survey is needed. Sample size will depend upon the condition of interest. Xerophthalmia (the clinical manifestation of VAD) is relatively uncommon in populations, and a large sample size is required to capture its occurrence. Smaller population samples can be used if subclinical indicators are the criteria of interest: low serum retinol levels, or abnormal relative dose response rates (RDR).

Treatment

Rapid improvement of the vitamin A status of individuals is critical in cases of xerophthalmia, severe infectious episodes (particularly measles, persistent diarrheal disease and dysentery, and acute respiratory tract infections), and severe protein-energy malnutrition. This is accomplished by (in general) oral administration of massive amounts of vitamin A in the form of retinyl palmitate or retinyl acetate capsules. Table C-2 in Annex C contains the suggested treatment schedule.

Prevention

The long-term goal of any VAD prevention program is the regular, adequate dietary intake of vitamin A by all groups in a population. In the short-term, emergency measures (as outlined above) to prevent VAD from becoming severe enough to cause ocular destruction or increased mortality may be necessary. The three most common intervention strategies to prevent VAD include increased dietary intake of vitamin A-rich foods, fortification of foods with vitamin A and periodic pharmaceutical supplementation. Generally, varying combinations (which may change over time) of all three strategies are needed.
Dietary intake/diversification

For children 0 – < 6 months, breastmilk is the best source of vitamin A. Because maternal vitamin A status determines the adequacy of breastmilk levels, targeting recently delivered mothers (within 6–8 weeks) for supplementation with a high dose vitamin A capsule (200,000 IU) in areas where diets are known to be low in vitamin A is an effective VAD prevention strategy. Support continued breastfeeding through the second year of life in combination with appropriate, vitamin A-rich foods (as well as adequate amounts of fat in children’s diet to enhance absorption of vitamin A) for children 6 months and older.

Modification of older children’s diets may also be a feasible option for increasing vitamin A consumption, often without increasing household food expenditures. Well-planned and executed qualitative studies are particularly important for the successful design and implementation of dietary modification strategies. Table C-3 in Annex C provides the recommended dietary requirements for vitamin A. Table C-4 gives illustrative food sources although regionally specific food composition tables will be needed to tailor effective strategies.

Food fortification

Food vehicles for potential fortification with vitamin A are listed in Table C-5, Annex C. Fortification of cereals, commercial weaning foods, and

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4. WHO (2004) recommends that mothers receive a high dose vitamin A supplement within 6 weeks of delivery. For breastfeeding mothers, the safe period extends to 8 weeks after delivery. Supplementation with vitamin A beyond this time-period is avoided to prevent any chance of harming a developing fetus accidentally (vitamin A, in large doses, presents teratogenic risks).
infant formulas with other micronutrients in addition to vitamin A has been accomplished but multiple fortification opportunities are still limited. Vitamin A fortificant products are fairly stable in modest heat but must not be exposed to ultraviolet light or oxygen. They do best in an alkaline environment, and fortificants are manufactured with antioxidants as stabilizing agents. The costs of fortifying foods with vitamin A vary. Table C-5 provides a range of approximate costs.

Supplementation

Periodic supplementation (once every 4–6 months) with vitamin A is a successful strategy because of the liver storage mechanism for this micronutrient. Table C-6 in Annex C gives the suggested prophylaxis schedule. While the capsules themselves are relatively inexpensive (see Box C-2, Annex C), delivery systems may be costly. It is most efficient to distribute supplements through existing health care delivery systems such as national immunization programs. The relative costs of vitamin A supplementation have been estimated at $0.50 per person in South Asia (Bouis 2003). Additionally, vitamin A supplementation of children under 5 years costs US$9 per DALY earned (Institute of Medicine [IOM] 1998/World Bank 1994).

Toxicity issues

Vitamin A toxicity is generally classified into three levels: acute, chronic, and teratogenic. Acute toxicity occurs with one or several closely spaced large doses (100 x RDA\(^5\) in adults and 20 x RDA in children). Daily vitamin

5. Recommended Daily Allowances (RDAs) are synonymous with Recommended Nutrient Intakes. These are the levels of nutrients thought to be high enough to meet the needs of nearly all the people within a similar group (see page 66 for an expanded discussion of recommended nutrient intakes). In the United States, RDAs are being replaced by Dietary Reference Intakes (DRIs). The DRIs shift the focus—and the recommended nutrient requirements—from avoidance of nutrient deficiency disorders to the prevention of chronic diseases. For example, calcium DRI requirements are higher than the old RDA in order to avert osteoporosis.
A intakes of 12,000–600,000 IU in children and 50,000–1,000,000 IU in adults can create chronic toxicity. Symptoms of vitamin A toxicity include bulging fontanels (in infants), headaches, vomiting, seizures, changes in mental activity, and other evidence of increased intracranial pressure.

Teratogenic toxicity is associated with large supplemental doses of vitamin A in pregnancy and results in birth defects. As a result of these associations, pregnant women are recommended to take no more than 10,000 IU daily during pregnancy. Large dose supplementation to women of reproductive age is not recommended (except within 1–2 months post partum as noted in footnote 4).

**Iodine**

*Functional importance*

Human beings need iodine in order to produce thyroid hormones. These in turn assist the body in the development and function of the brain and nervous system as well as help to maintain body temperature regulation.

*Sources of iodine*

Iodine is found within the soil and in the sea, entering the body via food grown on iodine-replete soil or from the ocean. For populations living on soil from which most of the iodine has been leached (for example, mountainous regions and flood plains), fortification of food with iodine, pharmaceutical supplementation, or dietary diversification with food produced elsewhere (on iodine-replete soil) are essential interventions.

*Iodine deficiency*

While iodine deficiency can affect children at each stage of rapid growth (as infants, young children, and adolescents), the negative impacts of iodine deficiency on behavioral and cognitive development are greatest
in utero. Maternal iodine deficiency in early pregnancy can result in irreversible cretinism\textsuperscript{6} in the child as well as miscarriages, stillbirths, and low birth weight babies. Among older school-age children, iodine-replete children do better on tests of mental and psychomotor performance than their iodine deficient peers. Intervention with supplements or fortified foods has produced mixed results for physical and mental performance among school-age children, but correction of iodine deficiency before conception or in early pregnancy unquestionably prevents severe cretinism and milder mental retardation due to iodine deficiency. A frequent manifestation of iodine deficiency in both children and adults is the enlargement of the thyroid gland, or goiter. Apathy and lethargy also appear as symptoms of iodine deficiency disorders (IDD).

**Magnitude of the problem**

WHO, UNICEF and the International Council for the Control of Iodine Deficiency Disorders (ICCIDD) estimate that approximately one-third of the world’s population lives in iodine deficient environments. Globally, iodine deficiency is the single largest determinant of preventable brain damage and mental retardation. Close to 120 countries have documented IDD as a problem and approximately 11 million people have overt cretinism. Even more widespread is the range of less obvious iodine deficiency disorders; it is estimated that 2 billion people are exposed to IDD (WHO—General Assembly Speech, 2002). Women are more at risk for iodine deficiency than men, and infants, children, adolescents, and pregnant or lactating women are the population segments of greatest concern for intervention.

\textsuperscript{6} Cretinism is more likely when maternal iodine intakes are below 25 µg/day (normal intakes are 100–150 µg/day). It presents as a range of symptoms including mental retardation, deaf-mutism, spasticity, dwarfism, and short life expectancy.
**IDD surveillance issues**

When selecting the target group for IDD surveillance activities, vulnerability, representativeness, and accessibility must be taken into account (WHO/ICCIDD/UNICEF, 2001). While women of reproductive age should receive top priority for intervention, school-age children are often the target group for surveillance because of their accessibility through the schools. School-age children are at high risk for negative impacts from IDD, they reflect the current status of iodine nutrition, and they can be used for surveillance of other health problems such as iron deficiency and helminth infections (they are not a good surveillance target group for VAD or child growth using anthropometry.) Pregnant women attending prenatal health clinics are another potentially efficient target group for surveillance, although in both cases, non-attendees introduce uncertainty about representativeness.

There are two main purposes of IDD surveillance: To 1) derive prevalence estimates, and 2) identify high prevalence areas for intensive intervention efforts. Cluster sampling—a process in which sampling units are made up of clusters or groups of study units such as villages or schools—is the usual sampling methodology for IDD surveillance. See **Indicators for assessing iodine deficiency disorders and their control through salt iodization** (WHO/ICCIDD/UNICEF, 2001) for more details on selecting sample size and survey design.

**Assessment methodologies and indicators**

Indicators of IDD status are either clinical (thyroid size, cretinism) or biochemical (urinary iodine and thyroid-related hormones). When selecting which indicator(s) to use for surveillance purposes, it is important to consider acceptability (thyroid palpation is usually more accepted than drawing venous blood), storage and transport issues for specimens, availability of personnel for sample collection, and costs.
Using more than one parameter (a combination of clinical and biochemical measurements), is recommended. When severe deficiency is present, lowering rates of goiter and cretinism will be a likely focus of program activities. However, as a program continues, the emphasis will change to improving iodine intake. Indicators such as levels of salt iodization, iodized salt intake in a population, urinary iodine levels and normal thyroid function (as measured by thyroid stimulating hormone (TSH) levels in neonates) will then be of interest. As resources permit, WHO/UNICEF/ICCIDD suggest collecting a biochemical baseline for at least a portion of the population under surveillance.

**Biochemical indicators**

**Urinary iodine** levels based on early morning child or adult urine specimens (24-hour specimens are not necessary) provide an adequate assessment of a population’s—not an individual’s—iodine status. Only small amounts (0.5–1.0 ml) of urine are required, and well-sealed specimens can remain refrigerated for up to several months before analysis occurs. Results are expressed as μg iodine per liter of urine in 1999. A trained technician can process 150 specimens per day, and total instrument costs are approximately $3000 for the simplest analytical method. The total cost per specimen is estimated at $0.50–1.00 including labor (WHO/UNICEF/ICCIDD, 1994).

Two other biochemical indicators are substances found in the blood: **Thyroid stimulating hormone** (TSH) and **thyroglobulin** (Tg). An elevated TSH (used mainly as an indicator for neonates and infants) or Tg (used for both children and adults) level indicates low levels of iodine; this is of special concern for neonates or infants because of the rapid brain development.

7. The specimen is digested in chloric acid and the iodine content is measured in the reduction of ceric ammonium sulfate (yellow) to the cerous (colorless) form.
development occurring early in life. Blood specimens of only a few drops are collected and preserved as dried whole blood spots on filter paper. Blood spots are easily transported and are stable for up to 6 weeks, even under high temperatures and humidity. Costs associated with these indicators include the set-up of an enzyme-linked immunosorbant assay (ELISA) laboratory ($15,000), the hardware and software for processing up to 5000 tests/year ($5000) and the TSH assay kits which cost approximately $0.50–1.00/test. Labor costs are not included. The same lab and software/hardware equipment can be used for surveillance of other micronutrient and infectious diseases.

Clinical indicators

Palpating thyroid size, a more subjective indicator than biochemical parameters, is best done on children ages 6 to 12 (at younger ages, the thyroid gland is too small to easily perform palpation) and pregnant and lactating women. Where feasible, ultrasonography gives a more precise measurement of thyroid size. Portable ultrasound equipment is fairly sturdy, but requires a battery/generator or electricity to operate. In 1994, the necessary machinery cost approximately $12,000. The simplified, three-grade classification system for goiter size is found in Box C-3, Annex C. A total goiter rate (TGR, goiter grades 1 and 2) of 5% or more in school age children (ages 6–12) signals a public health problem. Due to the potentially high misclassification of goiter (sensitivity and specificity are low in grades 0 and 1 due to inter-observer variation), urine iodine levels should also be measured to confirm the presence or absence of problematic levels of iodine deficiency in a population.

How to determine whether a public health problem exists

As discussed above, WHO/UNICEF/ICCIDD recommend the combined use of at least one clinical and one biochemical indicator to determine that a population is experiencing serious conditions of iodine deficiency. Table C-7, Annex C provides a summary of the indicators and cut-offs for this purpose.
**Dietary requirements**

See Table C-8, Annex C.

**Intervention options**

Breastmilk from mothers with adequate iodine reserves provides enough iodine to prevent iodine deficiency disorders (IDD) in children up to 12 months old. After 12 months, in many regions of the world, iodine-depleted soil and lack of seafood in the diet dictate the need for long-term fortification of foodstuffs such as salt or water with iodine. Feeding behavior change efforts focus on the use of fortified foods such as salt, and in some areas, the avoidance of goitrogens. These are substances such as improperly processed cassava roots or leaves, some types of millet, cabbage, turnips, rapeseeds, mustard seeds, groundnuts, soybeans, water contaminated by geologically-derived goitrogens, and possibly *E. coli*, which naturally inhibit the functioning of the thyroid gland, causing IDD. In high prevalence areas of severe iodine deficiency, it may be necessary to undertake short-term supplementation with iodized oil, although universal fortification of salt (or some other food vehicle) is the preferred, most cost-effective intervention option.

**Treatment: Pharmaceutical supplementation**

Fortification of salt, water, or other food items is the preferred method to alleviate iodine deficiency. However, there may be areas in which severe deficiency exists and it is not possible to quickly organize universal fortification. Direct supplementation of individuals is generally done through the administration of oral (annually) or intramuscular (bi-annually) iodized oil. Recommended dose and frequency schedules are found in Table C-9, Annex C. Cost estimates for iodine capsules follow in Table C-10, Annex C. Further, it has been estimated that fortification with iodine costs US$8 per DALY saved (Institute of Medicine [IOM] 1998/World Bank 1994). WHO guidelines (WHO 1996) conclude that treating pregnant
women with iodine is safe at any stage of pregnancy, with maximum protection against endemic cretinism and neonatal hypothyroidism achieved when iodized oil is given before conception. (This means that the optimal target group is all women of reproductive age.)

**Prevention: Iodine fortification**

Average salt consumption levels range from 5–15g salt/day for children and adults. Desirable iodine intakes for adults range from 100–300 μg/day. Salt is fortified with enough potassium iodate to provide approximately 150 μg iodine/day. (See Box C-4, Annex C for a sample iodization level calculation.) A range of total costs for salt iodization in developing countries appears in Table C-11, Annex C.

**Indicators for IDD control programs**

In addition to the biochemical and clinical assessment indicators needed to identify the presence and magnitude of an iodine deficiency problem, indicators are needed to plan, monitor, and evaluate IDD control programs.

**Situation analysis data needs**

Most control programs center around efforts to iodize salt for universal consumption, with the possibility of supplementation interventions to combat severe deficiency used initially in the short-term. The first step is a situation analysis of salt available for human and animal consumption or food-grade salt. This encompasses all stages from production through distribution to actual consumption. Data requirements include all major salt producers/importers, production/import/export statistics, and

8. Food-grade salt contains at least 97% sodium chloride, excluding additives. All additives should be of food-grade quality. The production, packaging, storage, and transportation must not subject the salt to contamination. Contaminants such as arsenic, copper, lead, cadmium, and mercury should not exceed the levels of 0.5, 2, 0.5, and 0.1 mg/kg, respectively, as specified by the FAO/WHO Codex Alimentarius, 1992.
information on salt quality, packaging, transport and storage, retail marketing, prices, and household consumption.

Measuring iodine in salt

WHO/UNICEF/ICCIDD recommend updating these data approximately every two years in addition to monitoring iodine concentration levels at different points along the iodized salt distribution chain. There are two methods used to measure salt iodine levels. The **standard titration method** is more accurate but more expensive, requiring a laboratory and skilled technicians. It is recommended for checking factory-produced salt batches. The second method is measurement with a **rapid-test kit**. Simple to use in the field, they contain bottles of starch solution from which a drop is placed on the salt sample. A blue color develops in the presence of iodate (the preferred fortificant for warm, damp or tropical climates), with the intensity of the color indicating the iodine level up to 50 or 100 ppm. See Box C-5, Annex C for information on suppliers and costs for rapid-test kits. Although this latter method is only semi-quantitative, it can be used by schoolteachers for monitoring at the community level and even as a sample survey technique for salt iodization program.

Some iodine losses occur along the production/distribution chain for iodized salt. When monitoring iodine content of salt, establish standards for the expected iodine levels at varying production and distribution points; take into account climatic conditions, packaging, and customary daily salt consumption. Table C-12 in Annex C provides guidelines for monitoring iodine levels.

Process indicators for salt iodization

In addition to monitoring actual iodization levels of salt, it is important to have measurable process indicators for the program as a whole. WHO/UNICEF/ICCIDD recommendations for process indicators and criteria of adequacy are found in Table C-13, Annex C.
Monitoring overall efforts to eliminate IDD

WHO/UNICEF/ICCIDD suggests a combination of core indicators to monitor program progress toward eliminating IDD. A goal for the number of households consuming appropriately iodized salt monitors progress relating to the primary method for insuring prevention of IDD. Clinical (thyroid size) and biochemical (urinary iodine, TSH) indicator goals mark progress on physiological criteria for defining success in decreasing and ultimately eliminating IDD. WHO/UNICEF/ICCIDD goals are found in Table C-14, Annex C. Data from 2000–2003 on the percentage of homes consuming iodized salt are presented in Table C-14A, Annex C.

Toxicity issues

Daily iodine intakes in normal adults of up to 1000 μg appear to be safe and the likelihood of ingesting more than this amount is small. Salt is normally iodized at levels insuring an intake of 150–300 μg/day; daily consumption of 10g of salt containing 50 ppm of iodine would only add a maximum of 500 μg to other sources of iodine a person ingested. In susceptible individuals (a minority of adults, usually over 45, who have experienced long-standing iodine deficiency), cases of iodine-induced hyperthyroidism or iodine-induced thyrotoxicosis (IIT)—sometimes referred to as jodbasedow—will inevitably occur when a previously iodine deficient area is provided with iodine. The incidence of IIT increases for several years (in some studies the incidence doubled) after the introduction of iodine but then decreases, often to levels below those present before iodization (Hetzel and Pandav, 1996). It can be prevented in future generations only by correction of iodine deficiency.

The clinical course of IIT varies, but the most common and serious symptoms include rapid heartbeat, nervousness, weakness, heat intolerance, and weight loss. In some cases it is more severe and sustained and can be life threatening. The treatments are highly effective (including antithyroid drugs, radioactive iodine or surgery); the most serious problems develop only in the face of delayed diagnosis and treatment.
Because some IIT can be anticipated as iodine deficiency is corrected worldwide, it is important to educate public health officials and health care providers about the causes, symptoms, and treatment protocols. The public health establishment can reassure communities that treatment is effective and available, and that the condition is transient. It is essential that iodine deficiency prevention efforts (particularly salt fortification) are not sidetracked due to concerns over IIT. The community-wide benefits of improved iodine consumption outweigh the negative occurrence of IIT in a few individuals.

**Iron**

*Functional importance*

As an essential component of hemoglobin, iron is the key player in the transport of oxygen via red blood cells from the lungs to other body tissues and in the removal of carbon dioxide from cells to the lungs. Iron has a role in healthy physical growth, the immune system, reproductive outcomes, and in cognitive performance.

*Iron bioavailability*

The bioavailability of dietary iron (including low consumption of iron absorption-enhancers and high consumption of iron absorption-inhibitors⁹) is a more important cause of iron deficiency than the amount of iron in the diet. The absorption of iron in food depends on a number of factors. The body tightly regulates iron metabolism and an individual's absorption of dietary iron is inversely related to his/her iron status. In addition, the form of iron in the diet influences the amount absorbed. Heme iron,

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⁹. Enhancers form stable, soluble complexes with iron, allowing for absorption by mucosal cells of the intestine. Inhibitors bind to iron molecules and form insoluble iron complexes that cannot be absorbed by the intestine.
present only in meat, fish, and poultry (MFP), is much better absorbed
than non-heme iron. Non-heme iron is found in grains, vegetables and
also in meat, fish, and poultry. Absorption of non-heme iron is enhanced
by ascorbic acid (vitamin C) and the simultaneous consumption of heme
iron. Dietary factors that inhibit the absorption of iron include carbonates,
oxalates, phosphates, and phytates found in whole grains, legumes, tea,
coffee, and certain vegetables. Tea consumed during meals can de-
crease the absorption of iron from the meal by as much as 50 percent
(Krause and Mahan, 1984). Cow’s milk and foods that cause allergic
reactions can cause microscopic bleeding in the gastrointestinal tract.

A diet of **low iron bioavailability** (typical in many developing country
settings) consists primarily of cereals, starchy roots, legumes, and little or
no MFP or foods containing ascorbic acid. This diet also contains signifi-
cant amounts of inhibitors and few promoters of iron absorption. Approxi-
ately 5 percent of the iron in the diet is absorbed. A diet providing 10
percent iron absorption (**medium bioavailability**) contains small amounts
of MFP and some vitamin C-rich foods. Regular consumption of inhibitors
such as tea, coffee, cereal fiber, beans, and high calcium foods may
contribute to low iron absorption in this diet (and in low and high
bioavailability diets as well). **High bioavailability** (15 percent iron absorp-
tion) indicates a diet containing MFP and vitamin C-rich foods. This diet
is routinely consumed in developed countries (Fairweather-Tait, 1995).

**Nutrient interactions**

There is recent evidence that the interaction of other nutrients affects iron
absorption and utilization. Vitamin A plays a role in the mobilization of
body iron stores and poor vitamin A status is associated with iron defi-
ciency anemia (IDA). High intake of calcium inhibits the absorption of
both heme and non-heme iron, and riboflavin (found in liver, meat, fish,
milk, eggs, wholegrain cereals, green leaves and legumes) deficiency
tends to coexist and interact with iron deficiency.
Iron deficiency and iron deficiency anemia

Iron deficiency and anemia are linked to a number of negative outcomes: Fetal growth retardation, perinatal mortality, compromised mental development, growth failure and poor physical development of young children, lowered physical activity and labor productivity, increased maternal morbidity, and higher risk of maternal mortality with severe anemia (Gillespie, 1998).

Iron deficiency is acknowledged to be the most common form of malnutrition in the world, affecting individuals in every country on the globe. Iron deficiency anemia (IDA) represents the most extreme form of iron deficiency, with an estimated 2 to 2.5 cases of iron deficiency for every case of IDA. WHO estimates that more than 2 billion people, or 40 percent of the world’s population, are iron deficient. Almost 50 percent of women and young children in developing countries have anemia. While iron deficiency is not the only cause of anemia, where there is a high prevalence of anemia, iron deficiency is usually the most common determinant. IDA is found most frequently (and most severely) in children ages 6–24 months and in women of reproductive age, but it is also found in low birth weight infants, older children, adolescents, adult men, and the elderly.

The United Nations Standing Committee on Nutrition (ACC/SCN, 2000) published the following ranked prevalences of anemia (WHO statistics) among pregnant women (Hb < 11g/dl) by region: South-East and South Asia (75%), Eastern Mediterranean (55%), Africa (51%), non-industrialized Western Pacific (43%), and non-industrialized Americas (35%). The Indian sub-continent alone accounts for nearly half the global total number of anemic women.

Determinants of iron deficiency

Iron balance in the body is determined by the body’s iron stores, iron absorption, and iron loss. Individual iron requirements are determined by the body’s needs for growth, pregnancy, and iron losses. The highest
prevalences of iron deficiency—found in infants, young children, adolescent boys and girls, and reproductive age women—reflect the iron demands of growth, menstrual blood loss in non-pregnant women, and the expanding red blood cell volume and maternal and fetal tissue development of pregnancy. Parasitic diseases such as hookworm infestation, *Schistosoma*, whipworm and amebiasis cause excessive iron loss, and iron utilization is impaired during chronic infection (malaria, chronic diarrheal disease).

**Assessing iron status: Hemoglobin and hematocrit**

The most common assessment indicators for iron deficiency anemia are hemoglobin (Hb) or hematocrit (Hct) levels. Although both indicators lack sensitivity, they are simple and inexpensive tests to perform, and therefore amenable to field setting use. While anemia is not a specific indicator of iron deficiency, in most developing country settings a high prevalence of anemia is correlated with a high prevalence of iron deficiency. Definitive evidence of this can be gathered through monitoring Hb or Hct response to iron supplementation. A 1 g/dL increase in Hb after 1–2 months of supplementation is indicative of iron deficiency (WHO, 1968 in Gillespie, 1998). Tables C-15/16, Annex C give Hb and Hct cut-offs for anemia by specific population subgroups.

**Equipment for hemoglobin and hematocrit assessment**

Currently, hemoglobin concentrations are best assessed using the battery operated photometer by a HemoCue. A HemoCue system is

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10. Hemoglobin is the component of red blood cells responsible for transport of oxygen to and carbon dioxide molecules from the body’s cells. Hematocrit is the volume percentage of red blood cells in whole blood. Hemoglobin levels are influenced by age, sex, race (for example, a subset of African Americans have consistently lower hemoglobin concentrations than Caucasians), and altitude (see Table C-16 in Annex C) (Johnson-Spear and Yip, 1994 and Dirren et al., 1994).
easily portable, accurate, simple to use, and does not require back-up laboratory services. The latest system can also data manage. The recurrent cost of the disposable cuvettes may be problematic however, for sustainable community-based assessment and monitoring of iron status. Depending upon the ongoing surveillance needs or the sample size requirements for a survey, it may be more economical to consider purchasing the more expensive hematofluorometer which does not have the additional and recurrent cost of cuvettes. In addition to the cost factor, once the cuvettes are unwrapped (they are supplied in packages of 200), they spoil quickly in hot, humid weather conditions.

Using a hand-cranked or electric microcentrifuge, hematocrit assessment is also relatively easy under field conditions although the results are less reliable than hemoglobin assessment. There is generally no reason to collect both hematocrit and hemoglobin data; one or the other indicator is sufficient for programming decisions and monitoring intervention effects (the rule of thumb is that the Hct is approximately 3 times the Hb). Hemoglobin or hematocrit assessment is recommended only for periodic surveys in the context of Bank-supported projects; individual screening within routine health services is generally not cost-effective.

**Hemoglobin distributions**

If data are available, it is useful to compare hemoglobin distributions of subgroups within a population. Poor dietary iron intake and/or bio-availability is a likely determinant of anemia when women and young children are disproportionately affected compared to men. If the hemoglobin distribution of both men and women are skewed to the left (toward the lower Hb values), it is important to look at pathological determinants such as malaria, hookworm or other infections (Gillespie, 1998).
Serum ferritin

Another blood component, serum ferritin\textsuperscript{11} (see Table C-17, Annex C), is the most accurate indicator of total body iron stores, and especially useful when the prevalence of anemia in a population is low. However, the lack of a simple field-based testing method and the elevation of serum ferritin in response to infection, negate its use in most settings where Bank-supported projects operate. Newer indicators—transferrin receptors—are affordable only in laboratory settings and lack international standardization.

Dietary assessment

In general, dietary assessment of iron intake is useful only as a complement to collection of Hb concentrations. This is due to the frequently poor correlation of iron intake from dietary studies and iron nutritional status without correcting for bioavailability. Dietary iron intake is however, closely linked to energy intake. Based on studies of Western diets, there are an estimated 6mg of iron per 1000 kcal, equivalent to a daily consumption of 8–18mg of iron by most adults in developed countries. In developing countries it is common to find higher daily intake levels ranging from 15–30mg iron. However, low bioavailability (much of the iron is in the form of iron soil contaminants) results in poor absorption, leading to higher prevalences of deficiency (Allen and Ahluwalia, 1997).

Iron requirements

Table C-18, Annex C presents daily absorbed iron requirements at various life cycle stages and Table C-19 contains guidelines on daily dietary

\textsuperscript{11} Ferritin is a protein containing iron that functions in iron storage, particularly in the liver and spleen. Serum ferritin levels are correlated with overall body stores of iron; as iron is depleted, serum ferritin levels drop.
iron requirements based on three types of diets (high, medium, and low iron bioavailability). These requirements were developed by a joint FAO/WHO Expert Consultation (1988). The US National Academy of Sciences released Recommended Dietary Allowances (RDA) which differ marginally from the FAO/WHO guidelines. The RDA for iron are found in Table C-20, Annex C. In both cases, the required amounts reflect the fact that only a percentage of iron ingested is actually absorbed.

Sources of dietary iron

Published data on the iron content of various foods are readily available but difficult to compare because of frequent contamination of foods (especially cereals and pulses) with extrinsic iron. Bioavailability and an individual consumer’s iron status will affect how much iron is ultimately absorbed. Tables C-21 and C-22, Annex C present estimates from several sources.

Intervention strategies

As with other micronutrient deficiency disorders, food-based strategies provide the most desirable and sustainable methods for preventing and controlling IDA. These include improving the quality of the diet for increased iron content and absorption, as well as fortification of staple foods with iron. The goal of these strategies is to make available foods that will result in an increased intake and absorption of dietary iron.

However, life cycle iron demands (as in pregnancy), lack of high bioavailability iron in the diet, and restricted access to fortified foods, make direct supplementation of many vulnerable individuals or groups with iron and folic acid12 a short-term and possibly long-term necessity.

12. Folic acid is a water-soluble vitamin essential for cellular replication and differentiation, including the formation of red and white blood cells. Recent studies have linked additional folic acid intake prior to conception with reduced risk of a recurrent neural
Even in developed countries, nearly all pregnant women require iron supplements to meet the increased iron demands of pregnancy. Depending upon the setting, it may also be important to treat or control parasitic diseases within a population as preventive and curative interventions for anemia.

**Preventing and treating anemia in pregnant women**

Anemia in pregnant women puts them at risk for a range of negative outcomes. Severely anemic women are at heightened risk of dying during childbirth (a conservative estimate—coming from hospital death records—of attributable risk of maternal mortality due to anemia is 20 percent in Africa and nearly 23 percent in Asia). Anemia is also directly related to risk of pre-term delivery, inadequate gestational weight gain and increased perinatal mortality. Anemic women are likely to give birth to children who have depleted iron stores. Anemic women also have less physical energy resulting in lowered work capacity and possibly less ability to provide optimal care and stimulation of their other children.

**Iron supplementation**

Food-based strategies will almost never provide adequate amounts of iron to meet the greatly elevated needs of pregnancy (approximately 1000 additional mg of iron), necessitating iron supplementation of tube defect pregnancy. Research has also demonstrated that hemoglobin levels during pregnancy show greater improvement when iron is administered with folic acid than when given alone. Folic acid is found in many foods. The best sources are liver, kidney, kidney and lima beans, and fresh dark-green vegetables (especially spinach, broccoli, and asparagus). Other good sources include fish, whole grain cereals, dried beans, and groundnuts. Nutrition intervention strategies can encourage shorter cooking and storage times to better conserve the folic acid found in foods. Women of reproductive age, whether menstruating or pregnant, are most at risk of folic acid deficiency because of blood loss and increased blood production demands. Folic acid requirements are also elevated by malaria.
pregnant women. Large-dose supplementation late in pregnancy is relatively inefficient and ineffective and cannot substitute for longer-term (throughout pregnancy), smaller dose supplementation. Table C-23 and Box C-6 in Annex C contain guidelines for supplementation of pregnant women with iron and folic acid and complementary parasite control measures.

**Screening vs. universal supplementation**

Biochemical screening of pregnant women to assess anemia incidence and severity is standard protocol in most resource-rich countries. This practice allows identification of those women for whom dietary sources plus daily supplementation with iron at recommended universal levels (in the case of the United States Centers for Disease Control’s 1998 recommendation, 30 mg iron/day) are not adequate to meet their iron needs during pregnancy. Corrective treatment is prescribed and women’s hemoglobin or hematocrit response can be monitored.

However, in the majority of countries in which the Bank works, it is not cost effective to routinely screen pregnant women using biochemical methods and examination of clinical signs is not sensitive enough to detect less than severe levels of anemia. Given a) the constraints to routine screening in resource-poor settings (lack of laboratory facilities, trained personnel, equipment, and low utilization of antenatal services in the most vulnerable populations), b) the nearly 100 percent prevalence of iron deficiency and c) high levels of anemia among women and children, all pregnant women and children 6 to 24 months need to receive presumptive iron supplementation treatment.

It is important however, to identify and treat women suffering from severe anemia, as these mother and infant pairs are at highest risk for morbidity and mortality. Primary health care workers need training on assessment of the clinical signs and treatment of this condition. In the absence of biochemical testing capabilities, clinical assessment of
pallor (examination of the conjunctiva of the eye, the nail beds, and the palm) will detect 50 percent or more of women with severe anemia in populations with high levels of anemia. These skills should be taught and performed when health workers have contact with pregnant and post-partum women.

**Iron nutriture in non-pregnant women and adolescent girls**

Building girls’ and women’s iron stores before pregnancy is an effective preventive measure but one which is often not included in health programs. Reaching the vulnerable population may be difficult and costly, especially in contexts where services to women are delivered through clinic-based prenatal care programs. In addition to improving iron status of adolescent girls, there is some evidence that supplementation may result in improved growth, both of pregnant adolescent and pre-pubertal girls, with subsequent reduced incidence of cephalopelvic disproportion (Gillespie, 1998). One way to reach this target group is to distribute iron tablets through schools. Girls not attending schools may be reached through other avenues such as women’s groups, peer groups, and youth groups. Iron supplementation and parasite control guidelines for these groups are found in Tables C-24 and C-25, Annex C.

**Preventing and treating anemia in young children**

Preventing and controlling anemia in young children is important because of the association of anemia with impaired cognitive development and physical activity. A recent review of the effects of undernutrition on children (Task Force on Nutrition and Behavioral Development of the International Dietary Energy Consultative Group, 1996) shows lower performance by anemic infants and toddlers on tests of mental and motor development relative to peers with normal Hb. Preschool and school age children with anemia also score lower on cognitive tests. Supplementing older children with anemia is clearly efficacious; improved performance on general intelligence tests as well as on tests for specific cognitive
processes resulted. Research suggests, however, that at least some of the effects of iron deficiency in infancy may be irreversible, making prevention of anemia during infancy a priority. Box 3-2 contains recommendations on anemia control strategies for young children.

Full-term infants are generally born with sufficient iron stores for the first six months of life when combined with the easily absorbed iron from breastmilk. Iron from fortified formula is not as easily absorbed as that from breastmilk (although it is usually sufficient) and infants fed unfortified animal milk are at high risk of iron deficiency. When iron-fortified complementary foods are not available, iron supplements are needed to meet the needs of rapidly growing young children between 6 and 24 months of age, and in areas of high anemia prevalence (> 40%), supplementation should continue through the second year of life. Table C-26 in Annex C contains

<table>
<thead>
<tr>
<th>Box 3-2: Anemia Prevention Strategies for Infants and Young Children</th>
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<tbody>
<tr>
<td>• Antenatal care including counseling on iron-rich foods, maternal iron supplementation</td>
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<tr>
<td>• 0 – &lt; 6 months, exclusive breastfeeding; iron supplementation for low birth weight and premature infants from approximately 2 months</td>
</tr>
<tr>
<td>• 6–24 months, continued breastfeeding, add iron-rich and iron-fortified complementary foods, malaria control, and iron supplements as needed</td>
</tr>
<tr>
<td>• &gt; 24 months, infectious disease control, deworming, and malaria control in addition to dietary interventions and iron supplements as needed</td>
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supplementation guidelines. Low birth weight infants have lower body iron stores from the outset, and are at risk of deficiency after 2 to 3 months; these children require iron supplementation from 2 to 3 months of age.

**Preventing and treating anemia in other population groups**

Preschool and school-age children, and other adults may benefit from iron supplementation interventions. Table C-24, Annex C presents recommendations on supplementation dosages for these groups. Complementary parasite control measures are found in Table C-25.

**Supplementation interventions: Issues of program success**

Iron intervention programs have proven difficult to implement successfully despite widespread consensus on the biological efficacy of the supplements. The main operational constraints in programs targeting pregnant women have been identified as:

- supplement supply, procurement and distribution problems,
- restricted access to, and minimal use of, antenatal care by pregnant women,
- poorly trained and motivated health workers leading to inadequate counseling of mothers, and
- low levels of compliance with the supplementation regimen by mothers.

While undesirable side effects and lack of understanding about symptoms and the consequences of anemia may cause noncompliance, iron tablet supply problems are usually the most frequently cited problem by program beneficiaries. To ensure program effectiveness, have:
• an adequate supply\textsuperscript{13} of high quality (stability, shelf life, color, smell) iron tablets,

• good population coverage (tablets reach all levels of the health system and community-based distribution is encouraged) and appropriate targeting to at-risk groups,

• qualitative research to determine barriers to taking iron tablets,

• well-trained, motivated, and approachable community-based staff,

• community demand and compliance generated in part by an effective communication strategy involving both men and women, and

• simple but effective monitoring systems for all levels of the program.

Costs

Costs for iron supplementation of pregnant women vary, depending on the local costs of the supply and delivery system, staff training, communication and education dissemination efforts, and monitoring and evaluation. The cost of the supplements is low: UNICEF-supplied ferrous sulphate tablets cost $1.87/1000 tablets, or $0.34/180 tablets (recommended total dosage/pregnancy 2003).

Complementary parasite control measures are low cost. Albendazole or Mebendazole cost as little as 0.02 US$ per tablet, and are usually given once each year. Praziquantel, used to treat schistosomiasis, costs 0.20 US$ per treatment (World Bank, 2003).

\textsuperscript{13} Stoltzfus and Dreyfuss (1998) suggest that an optimal tablet supply is 125\% of the number needed for supplementing the individuals in the target population.
**Dietary modification interventions**

Exclusive consumption of breastmilk should protect adequate birth weight children from conditions of iron deficiency for the first 6 months of life. As complementary foods are added to children's diets, they often are prepared in unhygienic conditions, have low iron content, high levels of iron absorption inhibitors, and low energy density. Added to these problems is the tendency in many cultures to delay the introduction of solid foods until well beyond six months. Perhaps the two most important dietary modifications are 1), the avoidance of tea and coffee in young children and the restriction of adult tea and coffee consumption to non-meal times and 2), the consumption of vitamin C-rich foods with meals (e.g., substitute lemonade for coffee). There is some suggestion that iron cookware may contribute to absorbed iron intake. As with any dietary change strategy, local beliefs and constraints need to be taken into account when designing a behavior change program. See Box 3-3 for diet-based improvements of iron status.

**Fortification of food with iron**

While iron fortification of different foods has been successfully implemented for close to 50 years, it is technically more difficult to achieve than salt iodization. And unlike iodine and vitamin A fortification, using a single fortified food vehicle realistically will only provide 20–40 percent of an individual's iron requirement. Iron can interact with other chemicals in food and change color, taste, texture, and storage properties. Those forms of iron least likely to alter the food vehicle are generally more poorly absorbed. Reduced iron, which is the cheapest iron fortificant, must be of sufficiently fine particle size (smaller than 7d sieve) to be absorbed, for instance. If a suitable food that is centrally processed and widely consumed can be fortified with iron, it provides an important, cost-effective, and sustainable method for addressing IDA.
Iron fortification must do more than restore iron that is lost to the milling process—it must deliver additional iron over and above what is available naturally. Food vehicles which have been successfully fortified include cereal flours (e.g., wheat and corn), bread, noodles, breakfast cereals, and fortified milk. Additionally, increasing the consumption of iron absorption enhancers (e.g., heme iron from meat and fish, ascorbic and citric acids from fresh fruit and vegetables) and reducing intakes of iron absorption inhibitors (e.g., polyphenols in legumes, tea, and coffee, phytates in some cereals, calcium in milk) can further enhance iron absorption. Eating iron fortified foods in combination with meals can also improve iron absorption. Support exclusive breastfeeding for the first six months of life, and introduce iron-rich/bioavailable complementary foods (including iron fortified cereals when available) in combination with sustained breastfeeding through the first two years. Increasing consumption of iron absorption enhancers and reducing intakes of iron absorption inhibitors during meals can also enhance iron absorption. Encouraging food processing methods that enhance iron absorption, such as germination, malting, and fermentation, can also be beneficial. Ensuring the adequate intake of complementary nutrients involved in iron absorption and metabolism such as amino acids (protein), vitamin A, folate, riboflavin, and vitamin B12 is also important. Animal products are the best source of these nutrients apart from folate which is found in green leafy vegetables and some fruits. (adapted from Gillespie, 1998)
UHT milk, infant formula, powdered skim milk, salt, sugar, curry powder, fish sauce, and soy sauce. Soft drinks and fatty foods are not advisable as iron fortified foods. See *Incorporating Nutrition into Project Design* (Toolkit #1), p.37, for general characteristics of suitable food vehicles.

**Iron fortificants**

When selecting a fortificant important considerations are the bioavailability of the iron source and interaction with the food vehicle. A compromise is usually struck between a fortificant that is less chemically reactive but more poorly absorbed and one that is more reactive (affecting stability, color, and odor of the food vehicle) but has higher bioavailability. Table C-27, Annex C offers information on a variety of food vehicles with a potential for fortification with iron and Table C-28, Annex C has detailed cost and bioavailability data for iron fortification of flours and common cereals.

**Safety**

Safety issues include the quantities of fortificant added to food, the expected intake of the fortified food by different populations, fortificant purity, and potential interactions with other food constituents (Gillespie, 1998). The US Food and Drug Administration (Code of Federal Regulations 1994) lists as GRAS (“generally recognized as safe”) the following iron fortificants: elemental iron, ferric phosphate, ferric pyrophosphate, ferric-sodium-pyrophosphate, ferrous gluconate, ferrous lactate, and ferrous sulphate. In 1999, the Joint FAO/WHO Expert Committee on Food Additives (JECFA) evaluated the benefits and potential health risks of iron-EDTA for use as an iron fortificant in food and concluded that, “Sodium iron EDTA could be considered safe when used in supervised food fortification programmes . . . .” Iron-EDTA is a focus of interest to the international nutrition community because it is chemically stable and reduces the inhibitory effect of wheat phytate and high bread-baking temperatures, making it well suited to foods that require long storage or high temperatures for processing. Sodium iron EDTA is absorbed two to three
times better than ferrous sulfate and does not cause rancidity or changes in food color. It has received approval from the FAO/WHO Codex Alimentarius Joint Committee on Food Additives as safe when used in iron-deficient populations. Sodium iron EDTA has limited application because it is relatively expensive and not widely produced, but it is possible to add disodium EDTA, which is less expensive, to ferrous sulfate and achieve the same advantage of improved iron absorption at lower cost. However, the negative effects of ferrous sulfate on food remain.

Cost of fortificants

Table C-29, Annex C pulls together approximate relative costs of various iron fortificants. Iron-EDTA is currently substantially more expensive than other iron sources, but this may decrease if there is an expanding market for the compound. Relative to supplementation, the per capita cost of fortification is low. Commercial iron fortification is estimated at $0.10 per person/per year (Bouis 2003).

Cost-effectiveness of IDA reduction

Interventions that successfully reduce the prevalence and severity of iron deficiency and IDA, particularly of adolescent girls and women, are among the most cost-effective in the armamentarium of public health. Fortification with iron costs US$4 per DALY saved (as compared to US$8 per DALY saved for iodine and US$29 per DALY saved for vitamin A). The costs of supplementation are also relatively low—providing pregnant women with supplemented iron costs US$13 per DALY earned (Institute of Medicine [IOM] 1998/World Bank 1994).

Iron overload

Debate on the dangers of iron overload resulting from either iron fortification or oral iron supplementation continues to stimulate research and discussion. The problem of iron overload appears to be restricted to
specific individuals with genetic iron metabolism problems, hemoglobin disorders, and extraordinary iron intake (e.g., from homemade beers brewed in iron pots). A paper prepared for UNICEF (in Gillespie, 1998) concludes that iron fortification will not lead to the development of iron overload among normal individuals. The efficient downregulation of dietary iron absorption applies to diets with high iron bioavailabilities, high heme iron content and to iron-fortified diets. In developed countries, those rare clinical problems among individuals are located through screening with biochemical tests (e.g., serum ferritin). Monitoring impact on iron status in the population is an important component of any iron intervention.

**Iron and malaria**

Malaria causes destruction of red blood cells and the subsequent storage of iron until new blood cells are synthesized. A single bout of malaria would cause only transient anemia. Recurrent malaria, however, overwhelms the body’s ability to make new red cells and results in anemia (often life-threatening severe anemia, especially in infants and women during their first pregnancy when malaria resistance is compromised). In response to the fact that the malaria parasite needs iron to survive, the body tightly binds iron so that the parasite cannot use it. Thus, there is some concern that iron supplementation might exacerbate malaria. Studies show conflicting results in terms of increased risk of morbidity as a result of iron supplementation, but it is clear that iron deficiency does not

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14. There are some conditions that predispose people to iron overload. Among a small minority of European extract populations, there are individuals with a homozygous defective gene that results in idiopathic hemochromatosis and a lack of the protective inhibition of iron absorption. Persons with chronic alcoholism and chronic liver disease may also have excessive absorption of iron. However, these are isolated medical issues and should be dealt with on an individual basis. The public health benefit of iron supplementation or fortification to an entire population should not be withheld on the grounds that a few individuals cannot benefit (as in the case of iodized salt or making available foods to which a few people have allergies).
protect against malaria, nor does iron supplementation at recommended dosages increase malaria virulence.

In individuals with sickle cell trait (these are individuals who are heterozygotes—homozygotes have sickle cell anemia and die quite early), approximately 40 percent of their hemoglobin is abnormal (shaped like a sickle) and they experience mild anemia as well as minor protection from malaria. Iron supplementation of individuals with sickle cell trait requires careful monitoring where malaria is endemic. Current guidance is to continue with iron deficiency control programs in developing countries, accompanied by monitoring efforts especially among known populations of concern.

Where P. falciparum malaria is endemic, if the affected person is a child younger than 5 years, give antimalarial treatment according to local recommendations. If the affected person is a pregnant woman, give curative antimalarial treatment at the first prenatal visit, followed by antimalarial prophylaxis according to local recommendations. For other affected individuals, examine blood film for malarial infection and treat if the film is positive. If a blood film cannot be made, give presumptive treatment (Stoltzfus and Dreyfuss, 1998).

Toxicity issues

Iron can be fatal to children in large doses (30 or more 60 mg tablets). Therefore it is critical to make sure that iron tablets are beyond the reach of children. Iron toxicity is treated by oral or intravenous administration of a compound that binds with iron and allows excretion of the excess mineral by the kidneys. Information concerning the potential for toxicity must be effectively communicated to IDA prevention program participants. When feasible, additional safety measures such as packing iron tablets in blister packs to reduce the likelihood of consuming an entire handful at one time should be considered.
Fortification with multiple micronutrients

Fortifying food vehicles with two or more micronutrients may provide the most cost-effective way to address micronutrient deficiencies. Multiple fortification of infant formulas, complementary (weaning) foods, and cereals has already proven successful. Micronutrient multimixes (usually containing thiamine, riboflavin, and niacin in addition to iron and/or vitamin A) are commercially available for cereals (mainly wheat). Double fortification of salt with iron and iodine is currently being field tested in both developing and developed country settings.

Zinc

Increasingly in the spotlight

While not one of the traditional “big three” micronutrients of concern to the public health community, zinc is gaining ground as a mineral with more extensive health benefits than were previously understood. Zinc deficiency prevalence data are more available and the impact of deficiency is receiving increased research attention.

Functional importance

Zinc's role in the body is multi-faceted, contributing to reproduction, growth, and the immune system functioning. Many enzymes require zinc and it is important in such fundamental processes as the metabolism of nucleic acids and the synthesis of proteins.

Dietary sources of zinc

Zinc is found in many foods, with animal products providing the most readily absorbed sources of the mineral. The best sources of highly
bioavailable zinc include red meat, liver, poultry, fish, eggs, crabs, and oysters. While cereals, legumes, and tubers do contain zinc, like iron, the bioavailability of zinc in plant-based foods is reduced by the phytates, fiber, and lignin (a component of vegetable fiber) present in the plant matrix. Specific food processing techniques such as soaking, germination, and/or fermentation also help to reduce the impact of zinc inhibitors. Cow’s milk is a poor source of zinc and also decreases the absorption of dietary zinc from other sources. The zinc in breastmilk is well absorbed and adequate for the first six months of life.

**Recommended dietary intake**

The average daily adult zinc intake in developed countries is 10–15 mg. The US RDAs are found in Table C-30, Annex C.

**Zinc deficiency**

Zinc deficiency is generally not found in isolation in individuals, but is one of many macro- and micronutrient deficiencies typical of a broadly deficient diet. Due to its important functional roles at the cellular level, inadequate zinc nutriture impacts on pregnancy, childbirth, and growth as well as decreasing immunocompetence and increasing infectious disease morbidity. Severe maternal zinc deficiency may lead to an inability to conceive, a high risk of spontaneous abortions, increased risk of preterm delivery, and possible neural tube defects in the neonate. Zinc deficiency is associated with increased incidence of low birth weight infants, reduced linear growth (stunting) and lower weight gain in children, and delayed sexual maturation (particularly in boys).

**Assessment of zinc status**

Zinc deficiency has no simple symptom or measurable indicator. At best one can a) measure zinc intake (although zinc is often absent from food
composition tables and bioavailability is affected by various dietary factors) and b) measure serum zinc using a cut-off for possible deficiency based on comparisons with other populations (for example, cut-offs from assessments of similar age, sex, fasting status and time of day). One can also measure deficiency based on the response of children’s (especially males) growth to zinc supplementation. More zinc will be needed for individuals consuming primarily cereal-based diets, and it appears that there is greater effect from small daily doses of zinc compared to higher dose supplements administered less frequently.

**Therapeutic effects of zinc**

Recent study results indicate that zinc supplementation appears to have a positive effect on growth and the reduction of diarrheal disease, acute lower respiratory illness, and possibly malarial incidence. Zinc may also positively affect psychomotor development.

**Interventions to prevent zinc deficiency**

As with iron, dietary diversification/modification efforts should attempt to increase intake of zinc-rich foods and decrease consumption of zinc inhibitors. The foods that promote and inhibit iron absorption do the same for zinc. Plant breeding strategies may be a possible means to increase the amount of bioavailable zinc in staple crops as well as zinc supplementation of targeted at-risk populations and fortification of food vehicles with zinc.

**Supplementation with zinc**

There is not yet agreement on zinc supplementation protocols. Studies of zinc’s interaction with other minerals provokes concern that zinc supplementation may exacerbate copper deficiency, and possibly increase the toxicity of lead and cadmium.
Fortification with zinc

The three most common zinc fortificants currently in use are zinc sulfate, zinc oxide, and zinc gluconate. They are equally bioavailable and have little effect on the shelf life or appearance of food. Zinc oxide is the least expensive and most frequently used zinc salt in the fortification of cereals.