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From Vitamin A to Zinc: Addressing Micronutrient Malnutrition



USAID's SPRING Project

Micronutrients, or vitamins and minerals needed in small quantities, are essential for good nutrition, proper growth and development, and overall health.⁸ Their deficiency contributes to extensive health problems and death throughout low-income countries, affecting millions of people globally each year.⁹ The negative impacts of these deficiencies, however, are not easily perceived because clinical signs appear only under extreme situations. The term “hidden hunger” is often used to characterize the difficulty in timely detection of the consequences of micronutrient deficiencies.¹⁰

For decades, USAID has been a leader in addressing micronutrient deficiencies, primarily through the targeted distribution of micronutrient supplements, food fortification and social and behavior change. Since the 1960s, three micronutrients—vitamin A, iron and iodine—have been the focus of USAID support because they are most often deficient; they also profoundly affect maternal and child survival, women’s health, IQ, educational achievement, adult productivity and overall resistance to illness, and can cause birth defects and blindness. Prevention and control of deficiencies of each of these micronutrients constitute three of the seven Essential Nutrition Actions.¹¹

In addition, zinc became a new priority in the 1990s when USAID-supported research indicated that zinc deficiency increases child morbidity and mortality during diarrhea episodes; USAID subsequently included zinc in its assistance for diarrheal disease management.

Attention to Micronutrients in USAID’s Early Years (1967-1975)

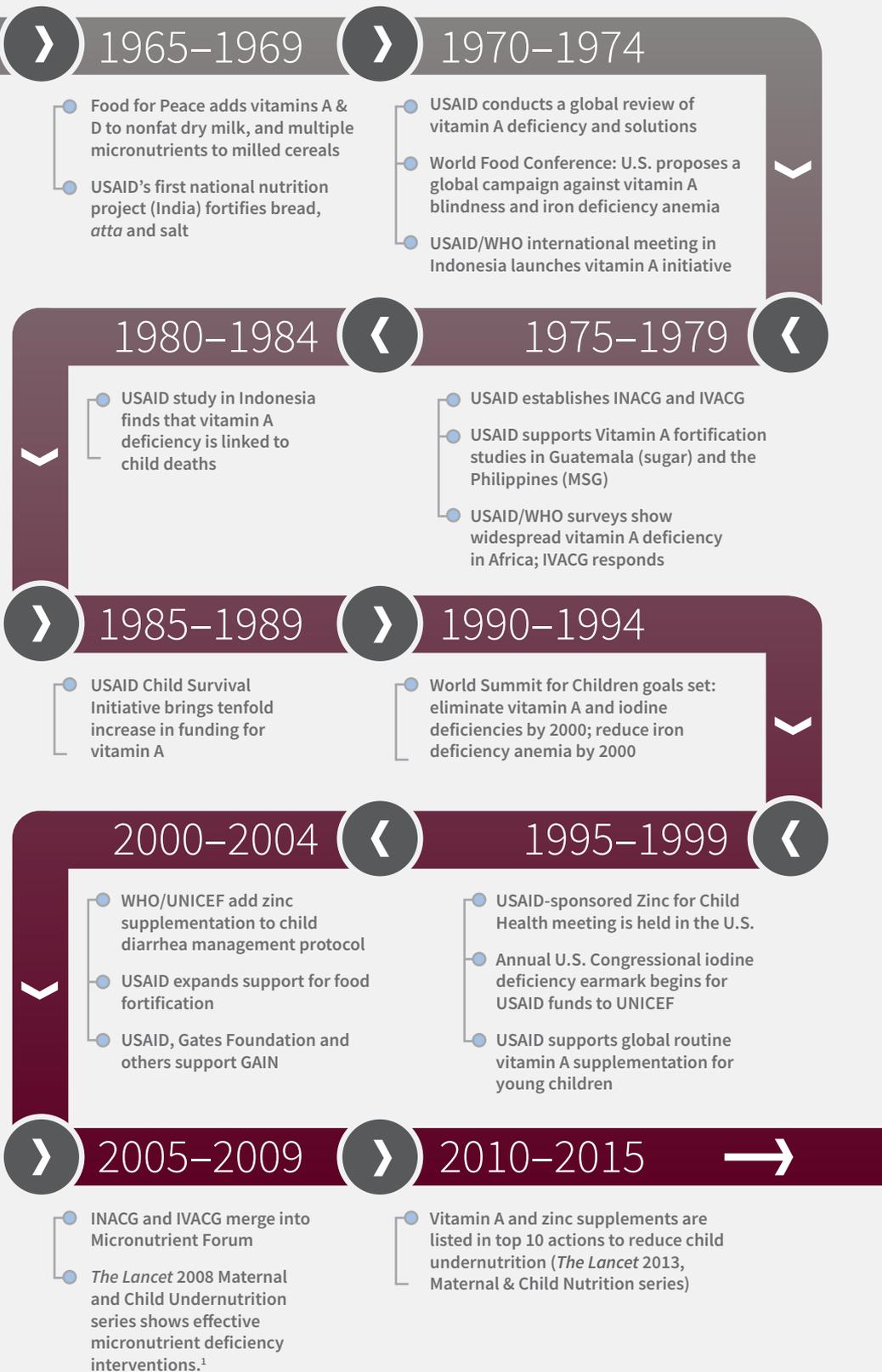
An early set of initiatives USAID undertook at the start of nutrition programming in the late 1960s and into the 1970s, in collaboration with USDA, was developing and testing low-cost food fortification technology options. Trials included tea with vitamin A in Pakistan, wheat with vitamin A in Bangladesh and with iron in Egypt, monosodium glutamate (MSG) with vitamin A in Indonesia, and salt with iodine in Pakistan.¹² A USAID nutrition program in India in the 1960s supported fortifying wheat bread and atta (whole wheat meal used to make chapatis, the flatbread staple) with multiple micronutrients and lysine (an essential amino acid to boost protein quality). The program also experimented with fortifying salt with iron and iodine (called double fortified salt). The major achievement of these partnerships among developing countries, USAID, USDA, U.S. universities and commercial fortificant companies was the invention of successful technologies for fortifying products with good consumer acceptability and nutritional value. Nevertheless, while the demonstration activities had positive results, the expectation that governments and the private sector would scale these up to national levels did not materialize in most cases. The challenges of who would pay for the fortification and how to secure the approval of governments and industry remained to be tackled.



What understanding of, and commitment to, micronutrients does exist in the world is due in large measure to the Agency’s pioneering efforts to have them understood as a key element of public health and to put their universal acceptance and availability within reach.

Source: Putnam, Eliot, et al., “Review of USAID’s Micronutrient Portfolio,” Arlington, Va., HTS Project, February 1997, p. xvi.

Milestones in Reducing Micronutrient Malnutrition



Key Global Results

- From 1998 to 2017, Vitamin A supplementation saved the lives of an estimated 1.25 million children.²
- Vitamin A supplementation programs started in more than 80 countries, and as of 2015, 26 countries had reached the target of 80 percent effective coverage.³
- From 2000 to 2015, the number of children receiving fully protective doses of vitamin A increased from 30 percent to 70 percent in priority countries (82 countries where vitamin A deficiency is a public health problem).⁴
- The number of households consuming iodized salt increased from 20 percent to 75 percent between 1990 and 2016, protecting millions of newborns from brain damage due to iodine deficiency disorders.⁵
- The virtual elimination of iodine deficiency disorders in the Americas was achieved in 2016.⁶

USAID Contributions to Global Results

- USAID support for field research led to the breakthrough discovery in Indonesia (mid-1980s) that vitamin A deficiency contributed to child deaths in addition to child blindness.
- Support for micronutrient supplementation has led to major increases in coverage.
- Assistance to scale up food fortification with micronutrients in 34 countries has resulted in such fortification now being widespread in low-income countries.⁷
- Since 1999, USAID support for universal salt iodization has benefitted 32 countries by protecting vulnerable individuals from serious, often life-long intellectual and developmental disability.
- USAID-funded studies on zinc for diarrhea treatment provided essential evidence leading to changes in diarrhea treatment protocols across international agencies.

By 1973, iron deficiency was determined to be the most prevalent micronutrient deficiency in low-income countries. In addition, numerous studies indicated that vitamin A deficiency could cause blindness in children.¹³ To gather more data on the latter, USAID commissioned a comprehensive international review of vitamin A deficiency.¹⁴ Studies on both of these micronutrients informed the U.S. Government's nutrition position at the 1974 World Food Conference in Rome. Then-U.S. Secretary of State Henry Kissinger challenged global partners to join the United States in ensuring food security and reducing malnutrition.¹⁵

“ The United States proposes an immediate campaign against two of the most prevalent and blighting effects of malnutrition: vitamin A blindness and iron-deficiency anemia... There are available and relatively inexpensive techniques which could have a substantial impact. The United States is ready to cooperate with developing countries and international donors to carry out the necessary programs.”

U.S. Secretary of State Henry Kissinger

The Rome conference marked an intensification of USAID efforts and investment to understand, assess, prevent and control micronutrient deficiencies worldwide. Within weeks, the WHO and USAID had convened a major technical meeting in Indonesia to launch a worldwide initiative on vitamin A.¹⁶ The following year, USAID formed the International Vitamin A Consultative Group (IVACG) and the International Nutritional Anemia Consultative Group (INACG) to stimulate research, inform global policy development, host technical meetings and provide technical guidance to policymakers and program managers through state-of-the-art publications, task force reports and policy statements.¹⁷ For the next three decades, USAID funded the IVACG and INACG secretariats. In 2006, these groups combined as the Micronutrient Forum, and USAID funding continued through 2010. As of 2018, the Micronutrient Forum was continuing its work as an international NGO to build consensus around evidence-based policies and programs that reduce micronutrient deficiencies.¹⁸

Research, Policy and Programming: Vitamin A, Iron, Iodine and Zinc Interventions

USAID has always addressed micronutrient deficiencies comprehensively and from a public health perspective. The Agency adopted a “from research to policy to programs” strategy, an initial approach to the concepts of implementation research and delivery science that followed.

Food Fortification

Fortifying foods with micronutrients is the practice of deliberately increasing the content of essential micronutrients to improve the nutritional quality of the food supply, and to provide a public health benefit with minimal risk to health.¹⁹ Mass fortification refers to the addition of one or more vitamins or minerals to processed foods and condiments that are commonly consumed, such as rice, oil, wheat flour, sugar and salt.

Fortification takes advantage of widely consumed, industrially processed or packaged food products, using food industry networks to distribute these products with additional micronutrients, without seeking to change a population's dietary patterns. Micronutrient fortificants are inexpensive, and fortification is cost-effective when implemented under the suitable conditions of production, enforcement, and consumer acceptance and use.

Throughout its history, USAID has employed the latest U.S. and international research and development technologies, research trials and protocols for the fortification of foods and condiments with vitamins and minerals. Domestically, Food for Peace has defined and implemented fortification specifications to improve the micronutrient content of the products USDA procures for food assistance. USAID began addressing micronutrient malnutrition by fortifying U.S. food aid with vitamins A and D in nonfat dry milk powder in 1965, and soon thereafter by adding multiple micronutrients to processed cereal products.

Over the years, expert reviews and feasibility studies illustrated the need for periodic updating of fortification specifications for food aid commodities. Equally important was establishing procedures to monitor the quality and quantity of micronutrients added to these foods by U.S. grain millers, a process initiated in 1994 with technical support and guidance from USAID implementing partners.²⁰ New requirements issued by USDA went into effect in 2000. The monitoring of micronutrients in U.S.-donated commodities represented a major advance in food aid quality.²¹

Internationally, USAID assisted 34 low-income countries with fortification of staple foods, beverages and condiments.²² Adding vitamin A to sugar has been particularly successful in Costa Rica, El Salvador, Guatemala, Honduras, Nicaragua, Malawi, Nigeria and Zambia.²³ Fortifying vegetable oil with vitamin A in Uganda, and wheat flour with multiple micronutrients in Nicaragua and the West/Bank Gaza, are other good examples of fortification projects in which effective food control systems were established to ensure sustainability.²⁴ National programs, such as in Malawi, Uganda and Kenya, launched with USAID investments, and including effective food control systems, have continued fortification independent of USAID funding.²⁵

The feasibility of fortifying rice, a key global staple, advanced through USAID's technical and cost analyses.²⁶ Working with the World Food Programme and USDA, USAID also developed rice fortification specifications that facilitated fortified rice being distributed in food assistance programs, including its own.²⁷ Another USAID-supported tool was the Food Fortification Formulator,²⁸ an Excel-based program to formulate micronutrient content



Malian refugees receive rice from a USAID-funded UN World Food Program project in Mbera refugee camp.

Agron Dragaj, UN World Food Program

and associated costs of potentially fortified staples, depending on the pattern of consumption of each population. A number of East, Central and Southern African countries used the tool to prepare fortification standards and regulations from 2008-2011, and for training and advocacy in that region. The Kazakh Academy of Nutrition used the tool from 2015-2017 to guide food fortification recommendations for the countries of Central Asia, Afghanistan and Pakistan.

Amidst the developing world's growth in both population and urbanization, mass fortification increasingly contributes to meeting micronutrient requirements. Fortifying Guatemalan sugar with vitamin A in the mid-1970s showed remarkable increases in serum retinol (an important marker and component of vitamin A) in preschool-age children, particularly in those with low initial levels.²⁹ Retinol levels in breastmilk also increased substantially, improving the vitamin A status of breastfed infants and young children.³⁰ USAID's leadership also has been critical in determining and clearly defining the food fortification roles and responsibilities of the public sector in public-private partnerships that are key to mass fortification success.³¹ The benefits of USAID's investment are reflected in the breadth of foods now being fortified globally.³²

Periodic updates to fortification specifications, as well as quality assurance and compliance monitoring, continue to be indispensable for maximizing the impact of food fortification on micronutrient malnutrition. USAID's technical assistance has steered national food fortification programs toward sustainability and self-reliance by: encouraging the participation of commercial food and pharmaceutical industries; setting a price low enough

to be compatible with the trade practices; establishing a government's commitment to maintain reliable enforcement systems; and periodically monitoring and evaluating program performance, quality, penetration and outcomes.³³

Vitamin A Supplementation

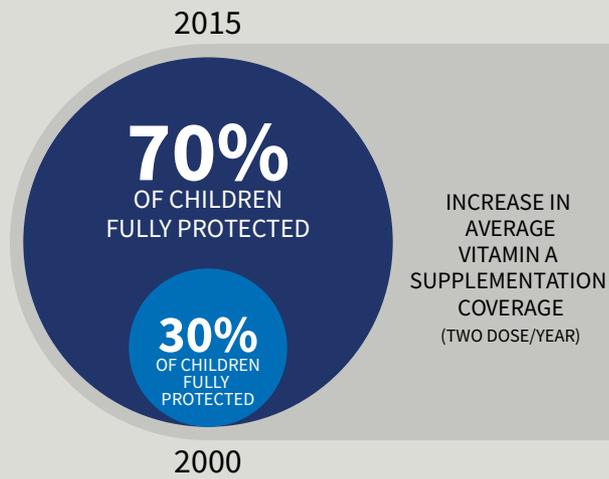
Beginning in 1976, USAID-supported studies in Indonesia revealed that severe vitamin A deficiency was the leading cause of childhood blindness in the country and, by extrapolation, in all of Southeast Asia. Importantly, vitamin A deficiency was found to be associated with a dramatic increase in risk of child death and exacerbated the severity of common infections, particularly measles. Also, for the first time, studies showed that preventing vitamin A deficiency through a large dose of vitamin A to children every 6 months could reduce their mortality by 34 percent.³⁴ The evidence of mortality reduction was so compelling, and the intervention so simple, that the findings were hailed as a breakthrough in international efforts to improve child survival. USAID, with assistance from other donors, funded additional major trials in Indonesia, Nepal, India, the Sudan and Ghana, with most reporting similar results.

In 1985, USAID began its Child Survival Initiative with a large increase in health funding, including a U.S. Congress earmark for vitamin A activities. This enabled USAID to increase its support for vitamin A activities tenfold.³⁵ Vitamin A supplementation in Asia and Africa became one of USAID's priority child survival interventions, along with breastfeeding, immunization and oral rehydration therapy. In other regions, like Central America, the mechanism of delivering vitamin A was through fortified foods.

In 1990, the U.N. hosted the World Summit for Children, a meeting of government representatives from over 150 countries focused on improving the health and well-being of children.³⁶ The Summit articulated specific nutrition goals, emphasizing the need to reduce iodine and vitamin A deficiencies in children and reduce iron deficiency anemia in women.³⁷ In 1993, a synthesis of findings from multi-country studies identified that an increased intake of vitamin A from a large, semiannual supplement significantly reduced mortality among children aged 6-59 months in areas of endemic vitamin A deficiency, aligning with the results from earlier USAID-supported studies in Indonesia.³⁸ The synthesis authors proposed that vitamin A (first referred to as the "anti-infective vitamin" based on early studies in the 1920s) likely contributed to child survival by reducing the severity of infectious diseases, particularly measles and diarrhea. Vitamin A supplementation has been broadly adopted in countries where vitamin A deficiency is endemic and no large-scale, alternative interventions exist.³⁹ Vitamin A supplementation has also provided an effective entry point in many countries for the semiannual delivery of other preventive services to young children, such as malaria control, deworming, immunization and nutrition counseling.

For women in deficient areas, vitamin A interventions may bring substantial health benefits. For example, USAID-funded research in Nepal found a 40

Increased Coverage of Children with Vitamin A Supplementation in 82 High Priority Countries, 2000 and 2015



Source: UNICEF, "Vitamin A Supplementation: A Statistical Snapshot,"
New York: UNICEF, 2016. <https://data.unicef.org/topic/nutrition/vitamin-a-deficiency/>



percent reduction in pregnancy-related mortality in women who took weekly doses of vitamin A or beta-carotene, a vitamin A precursor, during pregnancy, with the impact most apparent among women who were "night blind" (i.e., blindness in dim light caused by vitamin A deficiency).⁴⁰ Replication trials in Bangladesh⁴¹ and Ghana,⁴² however, did not show a significant reduction in maternal mortality, highlighting the importance of context-specific factors in determining the impact of interventions.

Building on USAID's investments in vitamin A research, policy development and programming, an array of international organizations and country governments became actively involved in vitamin A supplementation and fortification. USAID continues to support the vitamin A efforts of UNICEF, the Micronutrient Forum and the Global Alliance for Vitamin A.⁴³ The World Health Organization strongly recommends continuing implementation of the current policy of universal, twice-annual supplementation for children 6-59 months in countries where vitamin A deficiency is classified as a public health problem.⁴⁴ Vitamin A supplementation has also been incorporated into the Integrated Management of Childhood Illness guidelines and manuals as the standard treatment for severe measles throughout the world.⁴⁵

Because vitamin A supplementation programs were sometimes criticized for being too narrowly focused, USAID supported implementation research to develop the now widely used Child Health Day model of outreach from health facilities. These sessions deliver, along with vitamin A supplements, a package of preventive services such as immunizations, iron supplements for women or children, oral rehydration solution packets for diarrhea, de-worming, growth monitoring and promotion, nutrition education, health services referrals, family planning counseling and contraceptives all at the same place and time, making services conveniently accessible in the communities themselves.

In priority countries around the world, there was dramatic improvement in the full protection of children with vitamin A supplements between 2000 and 2015, particularly with sub-Saharan Africa. Annually during this period, UNICEF delivered about 500 million vitamin A supplements to children worldwide with USAID support. Sustaining high coverage is an ongoing challenge.⁴⁶

Iron Deficiency and Anemia Interventions

Anemia, or low levels of oxygen-transporting hemoglobin in the blood, has several causes. These include deficiencies of iron and vitamins such as folic acid and B-12, but also chronic and bone marrow diseases that interfere with the production of red blood cells, and sickle cell anemia. Risk factors for developing anemia include a diet lacking in certain vitamins and minerals; intestinal disorders; menstruation and pregnancy for women; advanced age; and family history.

The lack of iron is considered the most prevalent micronutrient deficiency and is presumed to be the leading cause of anemia. Iron deficiency, iron deficiency anemia, and other types of anemia cause a host of complications. During the first 2 years of life, low iron status can increase a child's risks for impaired cognitive, behavioral and motor development.⁴⁷ For women, iron deficiency



is associated with weakness, fatigue, reduced cognitive performance and diminished immune response. It is exacerbated by pregnancy and may increase the risk of low birth weight, delivery complications, and perinatal and maternal mortality.⁴⁸ In adults and children, iron deficiency can reduce the capacity for physical and mental activity.⁴⁹

Nonetheless, research, policy and action to reduce iron deficiency and anemia have been markedly more modest than attention to reducing vitamin A deficiency. This may be in part because the consequences of iron deficiency and anemia are less obvious than the two clear consequences of vitamin A deficiency (nutritional blindness and child death). Moreover, there is ongoing debate over the safety of iron supplementation in young children in areas where malaria infection is highly prevalent or intestinal infections are common.^{50,51}

USAID has taken steps toward meeting the challenges of iron deficiency by supporting supplementation and fortification, and important advocacy campaigns in national health agendas for anemia prevention and control for women and children. In addition, in more than 25 countries between 1995-2006, USAID efforts demonstrated that iron and folic acid supplementation could be made more effective with increased access and coverage and could reduce the prevalence of anemia.⁵² USAID continues this important work.

The most common food vehicle for iron fortification is wheat flour. USAID invested in research to optimize the bioavailability of iron and hence its absorption in the body from foods.⁵³ An important development was a new and improved form of iron for fortification: sodium-iron ethylenediaminetetraacetic acid (iron EDTA). USAID-sponsored studies contributed to the determination that iron EDTA is absorbed more efficiently than other sources of iron in flours, making it a desirable, alternative fortificant for whole flours.⁵⁴ Building on this research, USAID worked with the World Food Programme and the USDA to modify the specifications of fortified flours for food assistance, such as cornmeal, wheat and blended foods (e.g., Corn Soy Blend) to include iron EDTA in order to improve the utilization of iron.⁵⁵

Micronutrient powders (MNPs), sachets containing dry powder with micronutrients that can be sprinkled onto a child's porridge or other food, is another example of an innovation that received USAID support for initial testing. Efficacy studies have demonstrated that when the powders are used as recommended, iron deficiency anemia in children is reduced. Based on these studies, WHO recommended micronutrient powders as an alternative to traditional iron supplements.⁵⁶ Large programs distributing MNPs are ongoing. However, their sustainability and effectiveness at scale are still uncertain.⁵⁷

USAID projects have explored addressing the multiple causes of anemia through a broad-based, multi-sectoral approach, including preventing malaria, avoiding early pregnancy, promoting delayed umbilical cord clamping, and emphasizing dietary diversity to increase micronutrient intake (including iron), as well as deworming and agricultural production

of nutrient-rich foods. Such a collaborative approach permits the tailoring of a specific strategy for a particular geographic area, with major attention initially given to the primary factors contributing to anemia in the local context. Tools to support the multi-sectoral approach by countries⁵⁸ and districts⁵⁹ within countries were designed to estimate the relative importance of the causes of anemia and to plan programs accordingly.

Sustainable Elimination of Iodine Deficiency Disorders

Iodine deficiency disorders are the leading preventable cause of worldwide intellectual and developmental disabilities. Serious iodine deficiency during pregnancy retards fetal development, especially brain development, causing mental, motor and hearing deficits, including cretinism, a grave, irreversible form of mental retardation.⁶⁰ Through youth and adulthood, iodine deficiency can impair energy, work capacity, mental and physical function, and result in enlargement of the thyroid gland (goiter), among other consequences.⁶¹

To address this, iodine is most frequently delivered to populations through iodized salt. Since 1999, USAID has been supporting universal salt iodization through UNICEF to prevent the damage of iodine deficiency.⁶² During this period, 32 countries have benefitted from investments that help protect vulnerable individuals from serious, often life-long intellectual and developmental disability. The efforts of the Iodine Global Network,⁶³ with partners UNICEF, USAID, Kiwanis International, the Bill & Melinda Gates Foundation and the World Bank, have dramatically increased the production and consumption of iodized salt, protecting millions of newborns from learning disabilities caused by iodine deficiency.⁶⁴ In 2016, the Iodine Global Network celebrated the virtual elimination of iodine deficiency disorders in the Americas, and estimated that 750 million cases of goiter had been prevented worldwide since 1993 as a result of increased iodized salt consumption.⁶⁵ As of 2016, 130 countries supported salt iodization through mandatory or voluntary efforts by centralized private sector salt producers and sometimes through public sector food distribution schemes, as in India.⁶⁶ Also as of 2016, only 19 countries were classified as iodine deficient, showing tremendous progress from the 113 countries in this category in 1993.⁶⁷

Zinc and Diarrhea

The importance of zinc as an essential micronutrient for immune function, growth and development was discovered in the 1960s, but it was not until the 1980s that research focused on zinc loss in diarrhea and on zinc supplementation in diarrhea treatment. A USAID-funded meeting in 1996⁶⁸ summarized the known impact of zinc supplementation on child health outcomes, and outlined research priorities. Further study made clear that zinc supplementation, together with oral rehydration salts, reduces the duration and intensity of all forms of diarrhea.⁶⁹

USAID-funded studies provided the essential evidence base that led the World Health Organization and UNICEF to revise the treatment protocol for

diarrhea in 2004 to include zinc supplementation as well as administration of oral rehydration salts.⁷⁰ USAID implementing partners guided pharmaceutical companies, mainly in low-income countries, with protocols and technical support to meet UNICEF procurement standards and good manufacturing practices for zinc supplements. A regular and approved supply of dispersible zinc supplements is now widely available through international and national procurement systems.⁷¹

Playing the lead role among donors, USAID disseminated the findings of the benefit of providing zinc supplements during diarrhea episodes, and helped prepare advocacy, training and behavior change communication materials for rollout of the new, combined diarrhea management protocol. USAID also supported a number of NGOs, who quickly integrated the new protocol into their programs.⁷²

USAID Support to Country Micronutrient Programs and Global Efforts

From 1989 onward, USAID-funded micronutrient projects helped establish effective, sustainable, country-owned nutrition programs. USAID technical assistance to ministries of health and other entities built capacity and forged long-term relationships of trust with local institutions. Importantly, USAID and its implementing partners also advanced global learning and analysis of key accomplishments, and defined future directions based on evidence of what works in micronutrient programming.⁷³

Research funded through USAID has developed accurate yet practical methods for assessing vitamin A status and anemia; measuring supplementation coverage with vitamin A, iron and folic acid; and determining the presence

Anemia Interventions, Organized by Sector

NUTRITION



- Dietary diversification
- Dietary modification
- High-dose vitamin A supplementation for children
- Industrial fortification
- Iron-folic acid supplementation in women of reproductive age
- Maternal, infant, and young child nutrition
- Routine micronutrient interventions for children

GENETICS



- Counseling and management of genetic blood disorders

WATER, SANITATION AND HYGIENE



- Clean play spaces
- Handwashing
- Use of basic and safely managed sanitation facilities
- Use of safely managed drinking water sources
- Water treatment

REPRODUCTIVE HEALTH



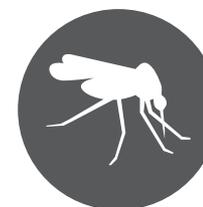
- Delayed cord clamping
- Family planning

AGRICULTURE



- Biofortification
- Increased production of nutrient-rich foods
- Promotion of food safety

DISEASE CONTROL



- Case management of malaria
- Deworming for schistosomiasis
- Deworming for soil-transmitted helminths
- Indoor residual spraying
- Intermittent preventive treatment during pregnancy
- Long-lasting insecticide treated bed nets

Source: USAID SPRING Project, *Understanding Anemia: Guidance for Conducting a Landscape Analysis*, 2nd edition, 2017.



A health worker in Egypt in 1988 gives a dehydrated child oral rehydration salts as part of a USAID-funded national program to control diarrheal diseases.

JSI/Egyptian National Control of Diarrheal Diseases Project



of iodized salt in households.⁷⁴ Through USAID's efforts, micronutrient-specific indicators are now included in the core modules of national Demographic and Health Surveys and the UNICEF Multiple Indicator Cluster Surveys. Key indicators include the coverage of vitamin A supplementation in children, iron supplementation in pregnant women, the presence of iodized salt in households, and the diversity or quality of complementary feeding behaviors.

USAID and the international nutrition community recognize the importance of private sector participation for achieving optimal human nutrition, especially the food and pharmaceutical industries. Thus, the Global Alliance for Improved Nutrition (GAIN) was launched at the United Nations 2002 Special Session of the General Assembly on Children with the aim of building partnerships with the private sector. USAID, together with the Bill & Melinda Gates Foundation and other sponsors, have supported GAIN since it was founded. GAIN has subsequently evolved into an international nongovernmental organization.⁷⁵

Addressing micronutrient malnutrition has proven attractive to governments in high-need countries. These interventions are relatively simple to implement, are supported by ample evidence of efficacy and have well-established and accepted models of delivery at scale. They also provide key entry points for integration into different services and programs, result in measurable impacts on important health and nutrition indicators, and are recognized by leading economists as very cost-effective.⁷⁶

USAID's major investments in micronutrients over the last 50 years have contributed substantially to this momentum and have yielded impressive results. USAID programming continues to support micronutrient fortification and supplementation for vulnerable populations as a high-impact intervention that enhances long-term health and productivity, and is working to facilitate increased country ownership of micronutrient programming to ensure these improved nutrition outcomes extend beyond the end of development assistance.