



# IDD NEWSLETTER

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# Cambodia closes in on IDD elimination

IDD has long been a significant public health problem in Cambodia. The Royal Government of Cambodia initiated a National Sub-Committee for Control of Iodine Deficiency Disorders in 1996 to fight this problem, focusing on Universal Salt Iodization (USI) as the primary strategy to improve iodine status.

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Although production of iodized salt started in 1999, there had been only limited success in producing it in large quantities. In 2000 the household consumption of iodized salt was only 12%. This was due to the existence of many small to medium-sized salt producers in Kampot and Kep provinces which were hard to bring under control and the lack of legislation requi-



ring them to iodize all their salt. The situation changed dramatically after the Sub-Decree No. 69 on “The Management of Iodized Salt Exploitation” was signed by the Prime Minister on 20 October 2003 and put into effect in October 2004. The Salt Producers Community of Kampot and Kep (SPCKK) was formed with participation of 167 salt producers. The SPCKK is overseeing most of production and distribution of iodized salt in the country. Some salt is also supplied (often illegally) from neighboring countries (Fig. 1).

**Cambodian iodized salt ensures optimal infant development**



The basis for production and supply of iodized salt in Cambodia is the production and harvesting of solar salt in Kampot and Kep provinces. Annual production of iodized salt ranges from 72,000 to 106,000 MT depending on weather conditions and the duration of the overcast period during the production season.

A first national school-based survey of iodized salt use was conducted in Cambodia in 2005. A total of 2,878 salt samples were tested with rapid test kits (RTK) of which 2,121 samples (73.7%) tested positive. The salt producing Kampot and Kep provinces had the lowest iodized salt consumption, at 19.3% and 27.7%, respectively, due to non-iodized salt coming from salt fields and storage barns. A lower use of iodized salt was also registered in some border provinces due to the illegal importation of non-iodized salt. Thus, despite significant progress, Cambodia had not reached the goal of IDD elimination by 2005.

To track further country progress, in 2008 the NSCIDD with UNICEF and ICCIDD support conducted a national school-based survey to assess iodized salt use and the iodine nutrition. In total, 2,329 school-children (8 to 10 years) were assessed. Household salt samples were identified as either “coarse” or “refined” salt and were tested for iodine with RTKs. Every third sample of salt was taken to a laboratory for quantitative iodine determination by titration. Urinary iodine (UI) determinations (a total of 1072 samples) were performed

in the laboratory of Mahidol University (Bangkok, Thailand).

### Coverage and quality of iodized salt in Cambodia

The performance of the salt iodization program in Cambodia has remained essentially unchanged over the last 3 years. Results of the 2008 survey show nearly the same proportion of households using iodized salt 73.7% as in 2005. The same provinces were identified as having an insufficient proportion of iodized salt at the household level. Thus, only 7.9% of households in Kep were using iodized salt (27.7% in 2005) and 27.8% in Kampot

the iodization requirement, both in terms of proportion iodized as well as in the iodine amount of the salt that was iodized, the median iodine content was 25 mg/kg for the coarse salt and 32 mg/kg for the “refined” salt. Also, while 73.7% salt samples collected in households across Cambodia were iodized, only 61.7% of salt samples were adequately iodized (defined as an iodine level of 15 ppm or more).

These data suggest that with the exception of the salt producing provinces of the South, the salt iodization program of Cambodia is providing sufficient iodine to almost the entire population.

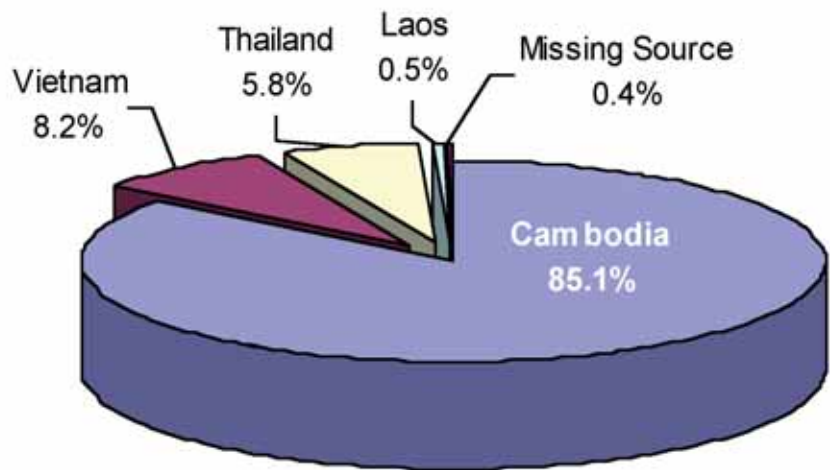


Figure 1: Main sources of iodized salt in Cambodia

(19.3% in 2005). Six provinces out of 24 had household coverage rates of 90% or better, and 13 were between 70 and 90% (Fig 2).

Importantly, coarse salt was reported as 63% iodized, and refined salt as 91% iodized. The “coarse” salt is produced from sea water by solar evaporation almost exclusively in the southern provinces Kampot and Kep. The “refined” salt is produced in Kampot province and by small producers of boiled salt in many provinces of Cambodia. Although the definition of “refined salt” may be somewhat subjective, it appears the salt of higher quality complies much better with

### Iodine nutrition of the Cambodia population

In the 2008 national survey, UI levels were determined in 1072 schoolchildren. The median UI level (221.5  $\mu\text{g/L}$ ) indicates iodine intake at the national level is slightly above the recommended range of 100-199  $\mu\text{g/L}$ . While this level of iodine intake is likely to provide an adequate intake for pregnant and lactating women, it may also pose a slight risk of more than adequate iodine intake in the population. Only 2.9% of urinary samples had iodine concentration  $<20 \mu\text{g/L}$ ; 8.9% of samples were  $<50 \mu\text{g/L}$  and more than 88% of urine samples had iodine concentration  $>100 \mu\text{g/L}$ .

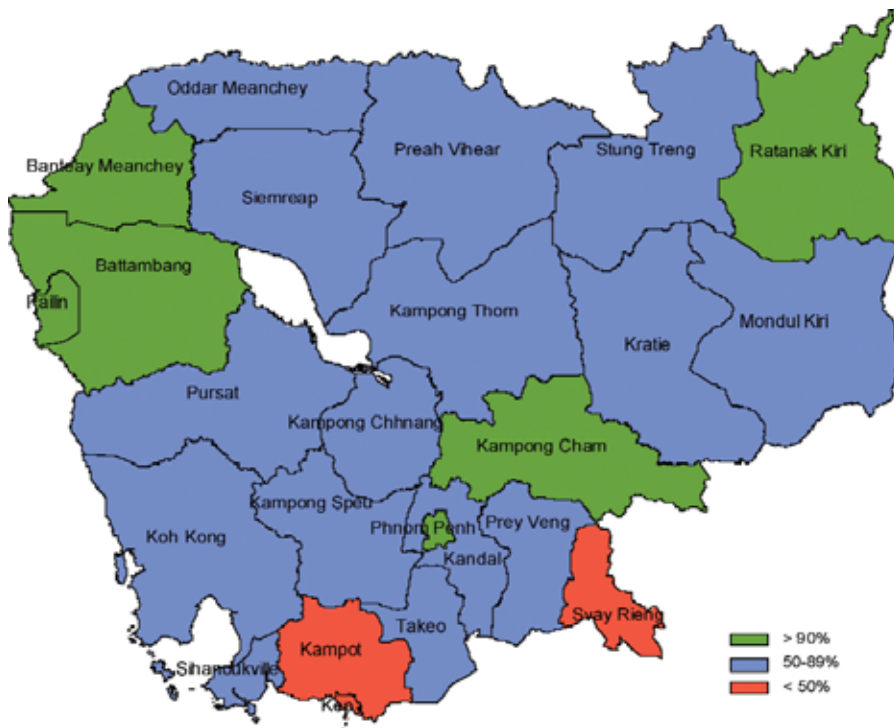


Figure 2: Percentage of households using iodized salt in different provinces of Cambodia (red color indicates <50% coverage; blue – 50-89%; green - > 90%).

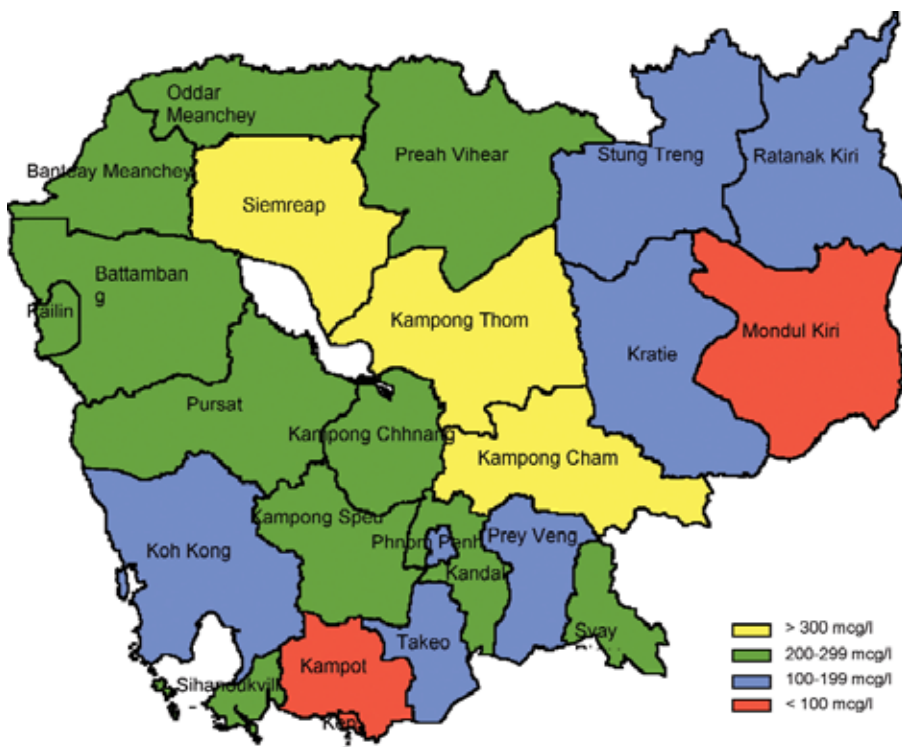


Figure 3: Median UI in the provinces of Cambodia

These UI data suggest the IDD control program in Cambodia is performing better than indicated by data on coverage of the population with iodized salt, based on salt testing with RTK. In only 3 provinces (Kep and Kampot in the South and Mondul Kiri in the East), the median UI was lower than 100 µg/L, indicating inadequate intake of iodine (Fig. 3).

The low median UIs in schoolchildren in Kep and Kampot is clearly associated with the lack of well iodized salt in these provinces. However, it is more difficult to explain the low UI in Mondul Kiri, because the proportion of households using iodized salt and the iodine concentrations in salt were identified as acceptable. At the same time, the median UIs in Svay Rieng, Kampong Chhnang, Siem Reap, Kandal and several other provinces were surprising in that a high UI is associated with a relatively short supply of iodized salt in the homes. The IDD situation in these provinces is more difficult to explain, and it may be attributable to failure of the RTK to detect the presence of iodine in the coarse salt common in Cambodia. Alternately, the contribution from other sources rich in iodine, e.g. fish sauce made with iodized salt, may play a role.

The results of the present survey indicate only 4.9% of the Cambodian population, specifically in Kampot and Kep provinces, have inadequate iodine nutrition while the rest of population (more than 95%) have a normal or more than sufficient supply of iodine. The UI results suggest the iodine intake of most of the Cambodia population is sufficient. In some regions it is likely at the high end of recommended intake, because for 10 provinces more than 40% of the urine samples had iodine levels >300 µg/L, the cut-off point to identify excessive intake of iodine.

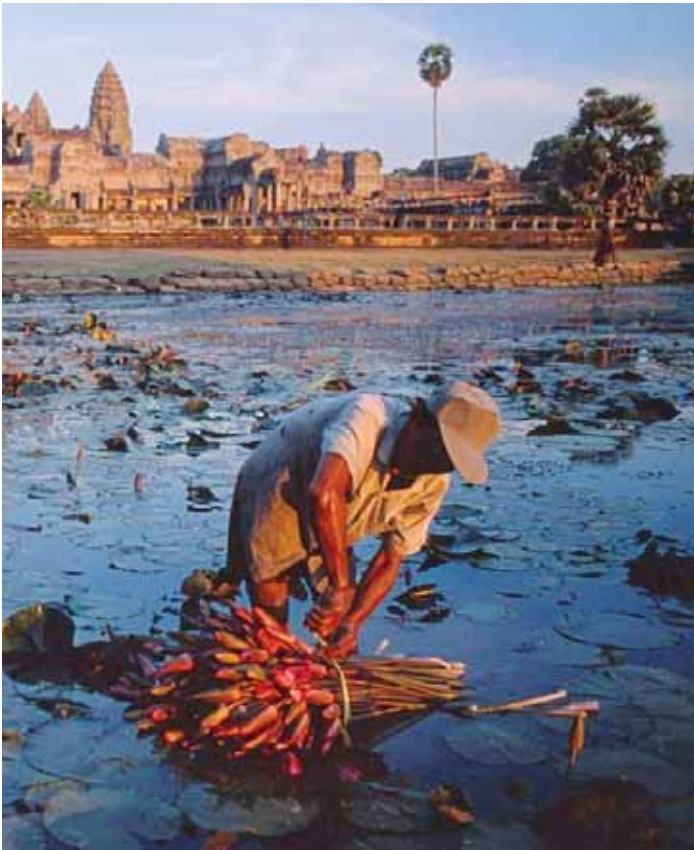


One of the reasons for normal or slightly elevated median UI in regions with a relatively low proportion of adequately iodized salt may be the overall high per capita salt consumption of the Cambodia population (directly and through condiments such as fish sauce). Also, the lack of a direct relationship between median UI and household consumption of iodized

reached a plateau of performance from the activities that have so far been implemented. Improvement of the coverage and quality of iodized salt in the provinces that fail to reach adequate coverage (Kampot and Kep) likely will require special targeted approaches and strategies. These provinces are major salt production regions, where non-iodized salt from eva-

### Acknowledgements

The authors wish to extend their thanks to field and laboratory personnel who participated in this survey, to UNICEF Cambodia (V. Berdaga), to Dr. O. Dary (AED, Washington, USA) and to Dr. K. Caldwell and Dr. A. Makhmudov (CDC, Atlanta, USA).



*Iodized salt increases productivity of Cambodian workers*

salt may be explained by the contribution of other food sources rich in iodine, such as fish sauce. However, the 2008 survey was designed and powered to provide data representative for entire population of Cambodia, not for separate provinces or groups of provinces, so it is difficult to draw conclusions on regional differences.

The similarity between the results of the 2008 survey and the data from the previous (2005) assessment implies the salt iodization program in Cambodia may have

poration ponds or storage barns likely enters the market. These limitations are not going to be solved by paying more attention to the iodization process, but can only be rectified by working with salt producers and the local communities to teach them the health risks of consuming non-iodized salt. While the iodine nutrition of the entire population of Cambodia is optimal, additional efforts are needed to improve the quality of production and iodization of domestically produced salt, especially in Kampot and Kep provinces.



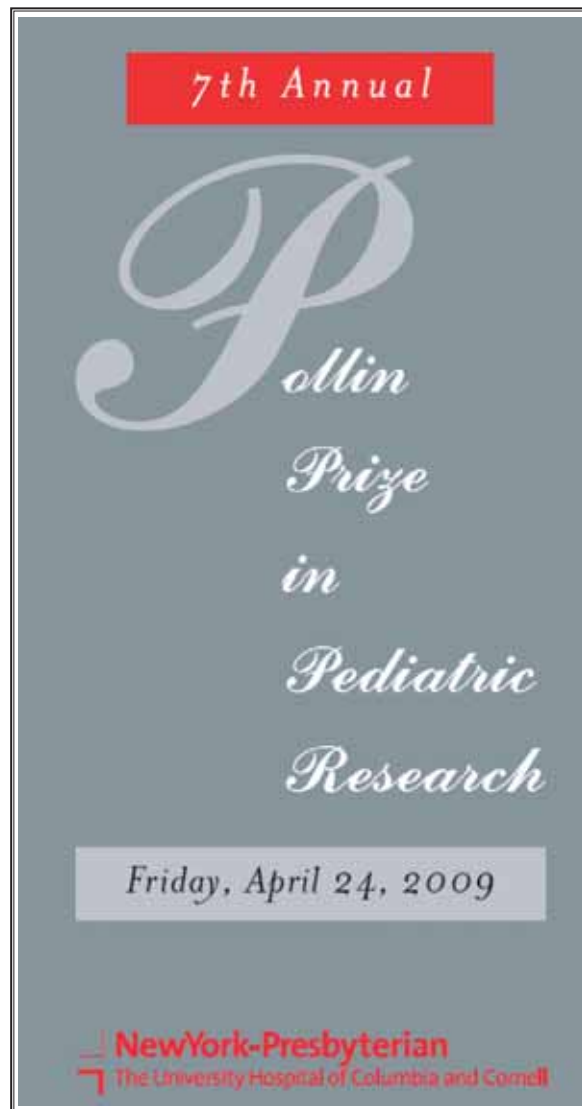
*Many small salt producers in Cambodia are still producing noniodized salt*

# Pollin Prize awarded to Basil Hetzel for his pioneering work on IDD

The 2009 Pollin Prize for Research in Pediatrics has been awarded to Basil S. Hetzel, M.D. for his discovery that maternal iodine deficiency can cause brain damage in newborns. It is estimated that Dr. Hetzel's work has protected nearly 80 million newborns from brain damage, and saved over one billion intelligence quotient points.

Basil S. Hetzel, M. D. was born in London in 1922 and was educated at King's College and St. Peter's College in Adelaide, Australia. After receiving his medical degree from the University of Adelaide, he pursued his postgraduate education and research in Adelaide (1945-51), New York (Fulbright Research Scholar 1951-54), and London (1954-55). He returned to the University of Adelaide to serve as Professor of Medicine (1956-68) and later spent seven years in the post of Foundation Professor of Social and Preventive Medicine at Monash University in Melbourne. In 1975, Dr. Hetzel joined the Commonwealth Scientific and Industrial Research Organization (CSIRO) as their first Chief of the Division of Human Nutrition.

From 1964 to 1972, he, along with a team of researchers in Papua New Guinea, established that severe brain damage could be prevented by correcting iodine deficiencies before pregnancy. Subsequent studies in animal models



confirmed the effect of severe maternal iodine deficiency on fetal brain development. Because of Dr. Hetzel's important research, the World Health Organization (WHO) now recognizes iodine deficiency as the most common preventable cause of brain damage in the world. Despite this understanding, it is believed

that each year nearly 41 million newborns from 130 countries are still at risk for brain damage caused by iodine deficiency. Dr. Hetzel has devoted his life to preventing needless brain damage in newborns. In 1985 he played a key role in establishing and then leading the ICCIDD, which has since grown into a multidisciplinary global network of 700 professionals from more than 100 countries. In 1995, he became Chairman of the ICCIDD and still serves as a senior advisor to the organization today.

In addition to his ground breaking work in iodine deficiency, Dr. Hetzel has published articles in more than 200 scientific publications and has worked as the author, editor, or co-editor of 18 books. His book, "The Story of Iodine Deficiency: A Challenge in International Nutrition" (1989) has been translated into French, Spanish, Chinese, Japanese, and Russian. Dr. Hetzel has been the recipient of numerous awards, including the Award for Distinguished Research Achievement from the International Association for the

Scientific Study of Intellectual Disability; the Living National Treasure Award, National Trust of Australia; Professor Kazue McLaren Leadership Achievement Award, from the Asia Pacific Academic Consortium in Public Health; and Centenary Medal, Federation of Australia.

# Did universal salt iodization help reduce the infant mortality rate in Nigeria?

*This article is a summary of a presentation given at the Nigerian Academy of Sciences Workshop: "Reducing maternal and infant mortality in Nigeria, bridging the gap from knowledge to action" at the Peiz Continental Hotel, Abuja-Nigeria, 24-26 March, 2009.*

**Daniel N. Lantum** ICCIDD Regional Coordinator for Africa



Nigeria is the most populous country in Africa. Between 1995 and 2006, the infant mortality rate in Nigeria decreased from 114‰ to 99‰. Although many factors contributed to the reduction in the infant mortality rate during this period, it is likely that IDD elimination played a role, as severe iodine deficiency may increase infant mortality (1).

At the 2007 Micronutrient Forum Meeting in Istanbul, Turkey, Nigeria was honored with the Universal Salt Iodization (USI) certification award, in recognition of the nation's pragmatic approach in combating endemic IDD through an aggressive salt iodization program (2). The WHO Regional Committee for Africa in its 58th session at Yaounde, Cameroon in 2008 recognized that "currently, only Nigeria has been certified as having achieved the goals of sustained elimination of IDD in the African Region. This achievement was possible because of a decentralized monitoring system, an efficient ultra-modern ana-

lytical laboratory, sensitized salt market, strict inspection and enforcement of universal salt iodization laws, intensive mass communication, social marketing, public-private partnership, collaboration with international organizations, and high-level advocacy" (3). The Nigerian action was an organized response to a major public health challenge.

Goiter was known to be endemic in parts of Nigeria, particularly in the Eastern, Western and Northern Regions. Oyenekwe et al. (4) comprehensively reviewed the pioneering studies of goiter prevalence in Nigeria. It was then widely believed goiter was due to low iodine content in the soil and foods, aggravated by goitrogens such as excessive cassava consumption.

With UNICEF support, in 1993 Egbuta conducted the National Baseline Survey of IDD in Nigeria and found a mean goiter rate of 20%, indicating moderate endemicity (5). Urinary iodine excretion (UI) was not measured in this survey. This was followed by a Federal Government Act stipulating that all food grade salt (both for human and animal consumption) should be iodized at 50 ppm. Compliance by the many Nigerian salt producers was excellent and they were monitored by the Standards Board of Nigeria (SON).

In 1995 (6), a Seven Africa Country Study on the impact of USI included Nigeria. Dan Lantum from ICCIDD led a national and international team, including SON, that studied iodization practices in industries and retailers. It also randomly selected two states with sentinel sites that had participated in the 1993 survey to assess

USI impact. One was Igarra Community in the Local Government Area of Edo, and the other was Enugu State, Omolopa Community. School children 5-12 years-old were studied. The team found USI was already well established and goiter rates were falling. Urine was collected for iodine measurement in Belgium and in parallel at the Federal Government Laboratory in Yaba.



*Iodized salt provides ample iodine for this Nigerian girl*

In 1998, Unicef supported a Second National Impact Survey, done under the leadership of Prof. Onyenekwe at the University of Nigeria Teaching Hospital (UNTH) Enugu (4). This included eleven States of Nigeria covering the four Public Health Ecologic Zones. It measured household availability of iodized salt, retail salt iodine levels with rapid test kits, the goiter rate and UI. It set up an Iodine Analysis Laboratory at the UNTH



Hospital. The results showed persistent progress in USI with decreasing goiter rates and rising UI. All salt samples were iodized, TGR was 11.8% and the median UI was 146.8µg/L (Table 1).

Maxiya Dixon (7), a Food Technologist working at International Institute for Tropical Agriculture (IITA) Ibandan was commissioned by the Federal Government with support of USAID to lead a national survey including children, mothers and pregnant women in 2001. Urine samples were analyzed in Cape Town at the Medical Research Council Laboratory. The results indicated IDD was virtually eliminated in Nigeria (Table 1).

In December 2002 (8), an IDD task force consisting of SON, the National Agency for Food and Drug Administration Control (NAFDAC) and the National Primary Health Care Development Agency (NPHCDA) carried out an assessment of production, marketing and consumption of iodized salt in Nigeria. The study concluded: "Overall, the findings of the survey indicated that in any given place in Nigeria, consumers can be more than 97.5% confident that when they buy branded salt, it is iodized. Furthermore, 98.3% of salt consumed at the household level is iodized, although 9.7% had lost sufficient iodine to drop below the 15ppm threshold. At the factory level, all the salt samples analyzed contained iodine at >15ppm.

**Table 1: Urinary iodine in Nigeria in 2003, by age/population group**

Group	N° Observations	Median µg/L	Mean µg/L	Std Error
Children under 5	2428	183.7	249.5	4.8
Mothers	3104	151.9	197.4	3.2
Pregnant Women	660	167.1	210.0	6.5

The retail level contained iodine at >15ppm in all but 2 States (Taraba and Ebonyi States) where 4%, and 25% respectively of the samples assayed contained <15ppm iodine." Thus the survey suggested USI had been generally sustained in Nigeria (9,10).

To further improve the situation, it was recommended:

1. The capacity of health and regulatory agencies is to be strengthened through training on quality control and monitoring, for institutionalized compliance monitoring.



*The Nigerian IDD control program is a model for all Africa*

2. The salt survey should be incorporated into NAFDAC's Annual Work Plan just like other inspectorate activities, and should be performed quarterly at the distribution level and annually at the retail level to ensure sustainability of monitoring.
3. As a routine activity, monitoring of the micronutrient deficiency control program should be integrated into other Health Service deliveries, eg. primary health care.
4. NAFDAC should conduct quantitative analysis of salt samples.

Current recommendations (2009):

1. Sustain the USI Program as it is
2. Intensify proper case clerking in hospitals, especially by obstetrics, neonatology and pediatrics
3. Intensify operational research in health care delivery
4. Increase diagnostic capacity of health institutions including laboratory infrastructure and scope of those laboratories
5. Intensify clinical research and reporting of hospital and health center statistics.
6. Assess improvements in IQ in children due to iodine malnutrition.
7. Investigate the possibility of goitrogenesis at Ekiti.
8. Endocrinologists and cardiologists should study the likelihood of iodine induced hyperthyroidism.

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In 2004, another National Survey was done, to assess USI impact and progress in general and in endemic zones. UI was measured in the new Iodine Laboratory at the University College Hospital Laboratory, Department of Chemical Pathology. The median UI again suggested virtual IDD elimination. The Global Network for Sustainable Elimination of IDD sent a team of external assessors to review the Nigerian USI/IDD situation and confirmed sustained elimination of IDD, a remarkable achievement for this large African country.

# Severe IDD in pregnancy in Northern Pakistan: a sentinel study

Hamida Ali and Peerzada Qasim Raza Siddiqui (Department of Physiology, University of Karachi), Junaid Mahmood Alam and Tehseen H Kazmi (Liaquat National Hospital Karachi) and Ghulam Mehdi (District Health Office, Khaplu Ghanche, Baltistan)



According to the WHO Global Database on Iodine Deficiency, Pakistan is a country struggling with severe iodine deficiency (1). In 1993-1994, a national survey of iodine status found a median urinary iodine concentration (UI) of 16  $\mu\text{g}/\text{L}$  and 90.4% of the population had a UI  $<100 \mu\text{g}/\text{L}$ . The total goiter prevalence was estimated to be 85% (1). About 17% of households were using iodized salt and 128 million people in Pakistan were at risk of iodine deficiency (2).

In 2005, Pakistan's Ministry of Health finalized the National Plan for Action with technical and financial assistance from the Micronutrient Initiative (MI). One of its highest priorities is to increase access to and use of adequately iodized salt in Pakistan (2). In 2008, the Nutritional Wing of the Ministry launched a project in 65 districts of Pakistan to enhance production of iodized salt in the country. Iodized salt production has increased from 17% to 70% in the districts where incidence of iodine deficiency is high (3).

In the Northern Areas of Pakistan, severe iodine deficiency has been recognized for a

century, particularly in Gilgit and Chitral (4). Baltistan, in the northeast of Pakistan, lies within the belt of IDD spreading from Bukhara and Samarkand in southern Soviet Union along the Himalayas and down through South East Asia to Papua New Guinea and New Britain (5).

From 1981-1986, Dr. Alex Stewart studied the prevalence of goiter and water iodine content in Baltistan. His studies demonstrated the prevalence of goiter in males was 34% and in females was 49%. Iodine content in water was low, with a mean value of 11.8 nmol/l, compared to mean water concentrations of iodine in other non-iodine deficient regions of 40 nmol/l (5). A Northern Areas Health Survey 1999 reported the goiter prevalence among various districts of the Northern Areas. The prevalence of grade 2 (visible) goiter was particularly high in the District of Ghanche Baltistan (Table 1) (6).

Because data on UI and thyroid function were not available for the Balti population, a sentinel study was conducted in four villages of Baltistan in the District of Ghanche in 2005. Blood and urine samples from 120 individuals were collected. Samples were collected from pregnant women (n=19), non-pregnant women aged 13-60 yrs (n=48),

males aged 13-60 yrs (n=45) and children 6-12 yrs (n=8).

**Urinary Iodine.** The results of the survey of urinary iodine are shown in Table 2. Of great concern, the data suggest pregnant women and children are severely iodine deficient. Males and females aged 13-60 years are moderately iodine deficient. Three quarters of the population has a UI  $<100 \mu\text{g}/\text{L}$ .

**Thyroid Function Tests.** The results of the analysis of total and free triiodothyronine (T3), total and free thyroxine (T4) and thyrotropin (TSH) are shown in Table 2. Pregnant women with severe iodine deficiency have abnormally high TSH and low FT4 concentrations. Thyroid hormone concentrations are within the normal range in females and males aged 13-60 years and in children.



Rugged mountains in northern Pakistan: a region of severe IDD





Most Pakistani children are iodine deficient increasing risk for poor development

This small sentinel study clearly demonstrates Baltistan remains severely iodine deficient. It also suggests thyroid function is impaired in pregnant women putting them at high risk of delivering an infant who may be brain damaged due to iodine deficiency. This highlights the urgent need to strengthen the national IDD control program in the region.

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**Table 1: Prevalence of goiter (%) among children 6-11 years in various districts of Northern Areas of Pakistan in 1999 (4).**

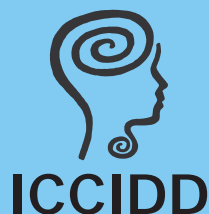
Goiter	Ghizar	Gilgit	Diamir	Skardu	Ghanche	All
Grade 0	97.1	89.8	87.8	60.0	37.7	77.8
Grade 1	2.9	8.7	12.2	29.5	39.8	16.4
Grade 2	0.0	1.5	0.0	10.5	22.5	5.8

**Table 2: Urinary iodine concentrations and thyroid function tests in Balti in 2005.**

	Median UI (µg/L)	T3 (ng/mL)	T4 (µg/dL)	TSH (mU/L)	FT3 (pg/mL)	FT4 (ng/mL)
Pregnant women	15	1.5	8.3	14.5	2.8	0.84
Non-pregnant women 13-60 years	37	1.3	6.6	2.6	3.2	1.01
Males 13-60 years	23	1.4	7.4	2.4	3.1	1.2
Children 6-12 years	18	1.4	8.5	2.4	3.9	1.3



Balti infants urgently need more iodine



INTERNATIONAL COUNCIL FOR CONTROL  
OF IODINE DEFICIENCY DISORDERS

## ICCID DECLARATION

# Importance and Safety of Optimizing Iodine Nutrition

Iodine deficiency is still prevalent world-wide. It can lead to goiter, thyroid dysfunction and is the main preventable cause of mental retardation globally.

Optimizing iodine intake is widely recognized as the most cost effective solution for achieving optimal intellectual development in addition to normalized thyroid function in iodine deficient areas.

The issue of the safety of increasing iodine intake has recently been raised based on occasional regional reports of detrimental side effects due to excessive amounts of iodine.

The current WHO recommended daily intake of iodine for adults is between 150 µg and 300 µg per day. The European Commission and the US Institute of Medicine have discussed tolerable upper

iodine intake for adults and have indicated intakes of 600 µg and 1100 µg per day, respectively.

Mild thyroid hyperfunction may occur following an increase of iodine intake within the recommended range as a consequence of pre-existing autonomous nodular goitre due to long standing iodine deficiency. This is a transient effect. The single relevant adverse effect is iodine induced overt hyperthyroidism (IIH), only observed in severely iodine deficient populations after a rapid introduction of excessive iodine supplementation which should and can be avoided.

Excessive iodine intake may lead to a transient small increase in the prevalence and incidence of subclinical hypothyroidism and thyroid autoimmunity, especially in older individuals.

Insufficient monitoring of salt iodine content and iodine intakes in populations increases the risk of iodine induced hyperthyroidism and other side effects. With sustained quality assurance and monitoring these can be almost entirely avoided.

While the overall incidence of thyroid cancer in populations does not appear to be influenced by iodine intake, a shift to less malignant types of thyroid cancer is widely recognized as a consequence of introducing iodine prophylaxis.

In conclusion, optimal iodine intake supported by adequate monitoring has been widely shown to improve the quality of various health aspects. The benefits of iodine supplementation far outweigh the relatively small risks of iodine excess.

# Urinary iodine concentrations indicate iodine deficiency in pregnant Thai women but iodine sufficiency in their school-aged children

Sueppong Gowachirapant Mahidol University, Thailand



*Pregnant Thai women are iodine deficient while their children have enough iodine*

The median urinary iodine concentration (UI) in school-aged children is recommended for assessment of iodine nutrition in populations. If the median UI is adequate in school-aged children, it is usually assumed iodine intakes are also adequate in the remaining population, including pregnant women. But iodine requirements are sharply increased during pregnancy. Recommended iodine intakes during pregnancy are 250 µg/d compared to 150 µg/d for nonpregnant women. The corresponding median urinary iodine concentration (UI) that indicates optimal iodine nutrition increases from 100-199 µg/L in nonpregnant women to 150-250 µg/L during pregnancy.

To clarify this issue, measuring UI from pairs of pregnant women and their school-aged children from the same family would be valuable. The value of matched pairs within a family is that both groups are sharing most meals from the same household food basket. Thus, a study of pairs can directly assess whether a diet that supplies adequate iodine to school-aged children also covers the needs of pregnant women in the household. In Thailand, although about 66% of

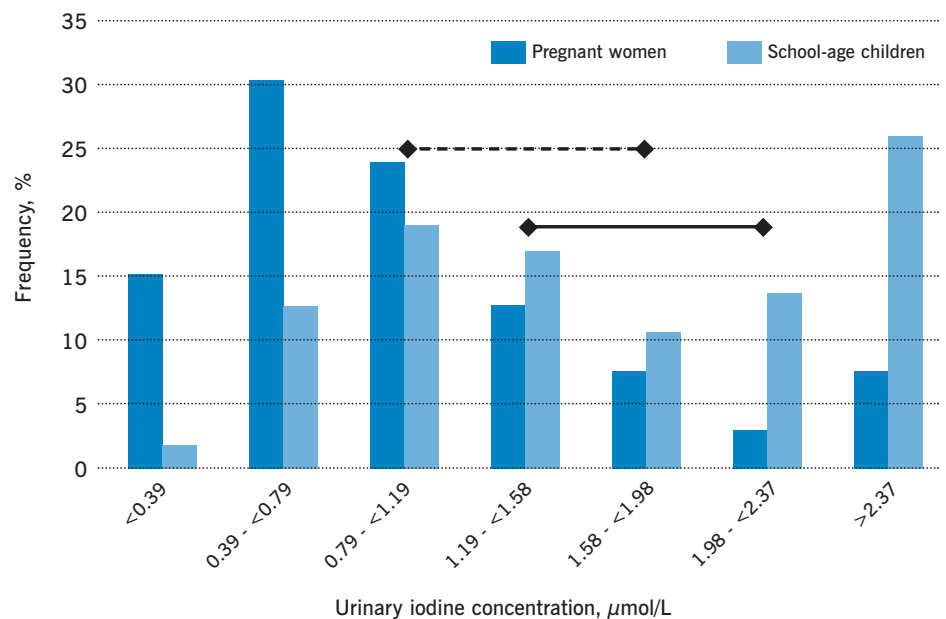
households use iodized salt, recent surveys have suggested iodine status in pregnancy may not be optimal. Therefore, the study question was: if the median UI is adequate in school-aged children, can one assume the median UI is also adequate in pregnant women? If so, then the median UI in school-aged children could continue to be used as a surrogate for monitoring iodine status in pregnancy; if not, then pregnant women would need to be directly monitored.

UI was measured in spot urine samples from pairs (n=302) of healthy pregnant mothers and their school-aged children in metropolitan Bangkok, Thailand. A dietary questionnaire was filled out. The median UI (range) in the pregnant women was 108 (11-558) µg/L and was lower than that of their school-aged children [200 (25-835) µg/L]

(p<0.001), indicating optimal iodine status in the children but mild-to-moderate iodine deficiency in their pregnant mothers. Estimated iodine intakes in the two groups were in the range of 130-170 µg/d. There was a modest positive correlation between UI in the pairs (r= 0.253, p<0.01). A higher frequency of seafood meals was a significant predictor of UI in both groups, but household use of iodized salt was not.

The findings indicate that in this region of Thailand the median UI in school-aged children may not be an adequate surrogate for monitoring iodine nutrition in pregnant women. These data need to be confirmed in other populations with varying dietary habits and iodine intake, but suggest adequate monitoring of IDD in populations should include specific monitoring of pregnant women.

**Figure 1: Frequency distribution of spot urinary iodine concentrations (µmol/L) in matched pairs of Thai pregnant women and their school-aged children (n=302). The recommended ranges for the median urinary iodine concentration for pregnant women (—) and children (---) are shown. Conversion from SI to conventional units, 0.0079 µmol/L=1 µg/L.**





# Research on iodine deficiency and goiter in the 19th and early 20th century

Michael B. Zimmermann ICCIDD Deputy Regional Coordinator for Western and Central Europe

I am satisfied. I have seen the principal features of Swiss scenery – Mount Blanc and the goiter – and now for home.

Mark Twain, 1880

## Introduction

In 1811, France was at war, and Bernard Courtois was producing saltpeter for gunpowder for Napoleon's army. He was burning seaweed to isolate sodium bicarbonate, and when he added sulfuric acid to the ash he produced an intense violet vapor that crystallized on cold surfaces. He sent the crystals to Gay-Lussac, who subsequently identified it as a new element, and named it iodine, from the Greek for 'violet'.

The ancient Greeks, including Galen, used the marine sponge to treat swollen glands. The sponge and dried seaweed remained a 'goiter cure' in the medical armamentarium through the Middle Ages. In 1813, learning of the discovery of iodine in seaweed, Coindet, a physician in Geneva, Switzerland, hypothesized the traditional treatment of goiter with seaweed or sponges was effective because of their iodine content. He began giving oral iodine tincture to goitrous patients at an initial daily dose at 165 mg. This provoked strong opposition among the medical profession; opponents claimed it was poisonous, and it was suggested "...Coindet would not leave his house for fear of being stoned in the street by his poisoned patients..." Although Coindet insisted his treatment was safe, the often acrimonious debate on the safety of iodine would continue into the early 20th century.



**Figure 1.**  
*Theodor Kocher, Swiss surgeon, won the Nobel Prize in medicine for his work on the physiology and pathology of the thyroid gland*



**Figure 2.**  
*In 1915, the rural Swiss general practitioner Bayard did the first dose-response trial of iodized salt to treat goiter in schoolchildren*

## First proposals to use iodized salt

The French chemist Boussingault, was the first to advocate prophylaxis with iodine-rich salt to prevent goiter. He measured iodine levels in rock and in salt deposits of the Andean region, and, in 1825, he reported villages in the province of Antioquia treated goiter with 'aceyte de sal', an acrid, 'marine smelling' fluid from the salt deposits. He demonstrated in 1835 that salt sent from goiter-free Antioquia to neighboring regions reduced goiter endemia. Boussingault was the first to recommend goiter prophylaxis with iodized salt; it would be nearly 100 years before their vision was realized!

## Chatin and goiter prophylaxis in France

The French chemist Chatin was the first to publish, in 1851, the hypothesis that iodine deficiency was the cause of goiter. Chatin, the director of the School of Pharmacy in Paris concluded: "Too low a concentration of iodine in the drinking waters of certain areas appears to be the principal cause of goiter." However, his estimates of food iodine content were about 10-fold too high and Chatin's work was greeted with great skepticism by the French Academy of Science.

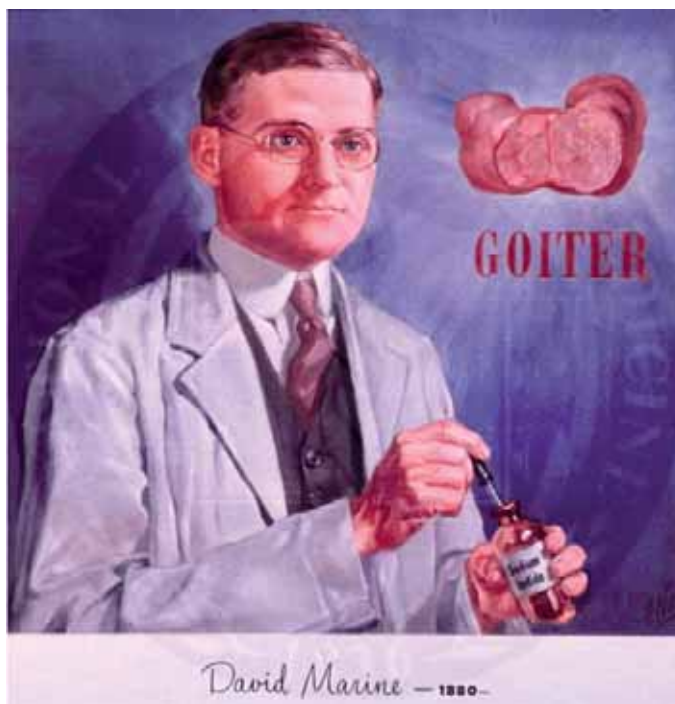
Despite this, French authorities, in three Departments where goiter was severe – Bas-Rhin, Seine-Inferieure and Haute-Savoie), began distributing iodine tablets and salt together with other prophylactic measures. In the prefect of Haute-Savoie, the cause of goiter was attributed by local physicians to drunkenness, dampness, poor hygiene and contaminated drinking water. Various measures were taken: large trees that prevented the entry of fresh air to villages were felled, wet streets were drained, the water tested for potability and school hygiene improved. In addition, iodized salt was distributed and schoolchildren were given iodine tablets daily. The program was clearly effective: in a survey of 5000 goitrous children, 80% were cured or improved by the iodine treatment.

However, because goiter exempted young men from unpopular military service in the French army, many parents, fearing their sons would be enlisted, were against iodine prophylaxis. Also, the doses of iodine administered both in table salt and tablets were too high: a concentration of 100-500 mg/kg was chosen for salt iodization, and the tablets, which were to be taken daily, contained 100 mg KI. This high dose of iodine was consistent with the enormous doses of iodine used to treat many diseases at the time (scrofula, syphilis, arthritis). While many people tolerated the high doses of iodine well, it likely precipitated iodine-induced hyperthyroidism in some individuals, and as a result, the program was discredited and discontinued.

### Myxedema and cretinism

Medical authorities recognized cretinism only occurred in areas of endemic goiter, but were puzzled by the fact that many cretins had an atrophic or absent thyroid gland, the opposite of goiter. A clue to this apparent paradox appeared when a related disease, myxedema, that resembled cretinism, was described by Ord in 1877 in London. In 1883, Semon suggested myxedema was due to a lack of activity of the thyroid after reading a report by the Swiss surgeon Kocher (Figure 1) describing myxedemic symptoms in patients after total thyroidectomy. British physicians began successfully treating myxedema with injections and/or oral doses of animal thyroid extracts; a 1893 review exclaimed "it was one of the greatest therapeutic triumphs of the age".

The link between goiter, myxedema and iodine was established when, in 1896, Baumann and Roos, working in Freiburg, Germany, digested animal thyroid glands and were surprised to isolate a residual insoluble fraction that was ca. 10% iodine. They found this substance, termed "thyroidine", to be effective in the treatment of both myxedema and goiter. They correctly surmised iodine itself was not therapeutically active, but had to be first incorporated into an organic molecule.



**Figure 3.** In 1916-17, the American physician David Marine conducted the first large-scale trials of iodine supplementation to prevent goiter in children in Akron, Ohio

### The Swiss introduce iodized salt

Switzerland's iodized salt program has been operating uninterrupted since 1922. Before its introduction, Switzerland was severely iodine deficient. For example, in 1800, a census ordered by Napoleon reported 4000 cretins among the 70,000 inhabitants of the Canton Valais, in the Swiss Alps. In 1918, the Swiss physician Bayard (Figure 2) did the first dose-response trial of iodine to treat goiter. He did this in Grachen, an isolated village at the base of the famous Matterhorn mountain in the Zermatt valley, reachable only by mule track. He gave iodized salt for six months to families in the village with 3 different iodine contents (3, 6 and 15 mg/kg). Bayard established that as little as 30 µg of iodine daily had a clear beneficial effect on goiter, and noted 'soft' diffuse goiters in children were more responsive than the nodular forms.

The Swiss Goiter Committee was formed in 1922. Initially, the committee cautiously advised the introduction of salt iodized at 1.9 to 3.75 mg/kg nationwide on a voluntary basis, a compromise between the proponents and opponents of iodized salt. The first canton in which iodized salt was introduced was Appenzell AR, in 1922, where salt was iodized at 7.5 mg/kg with spectacular results: newborn goiter disap-

peared, no new cretins were born, and goiters in children were reduced in size or disappeared.

### Iodine supplementation studies in the USA

At about the same time as the first Swiss iodine studies in 1915-1919, Marine and Kimball were introducing iodine prophylaxis in the Midwest region of the U.S. David Marine (Figure 3) trained at Johns Hopkins was appointed to a residency in pathology at Lakeside Hospital in Cleveland, Ohio. According to legend, he was surprised when asked on his first day what research problem he would like to work on. He had noticed several dogs with large goiters in the neighborhood and replied without much reflection he would like to work on thyroid disease. Marine sub-

sequently confirmed Baumann's finding that large goiters contained less total iodine than in healthy glands. The American surgeon Halsted had reported when part of the thyroid was resected, the remaining tissue increased in size. Marine extended this observation and suggested goiter was "a compensatory reaction to some deficiency" and it appeared "...iodine is the most important single factor...".

Marine realized goiter was a serious public health problem and in 1916 he planned to do an intervention with iodine in schoolchildren in Cleveland. However, the school board refused, concerned iodine could be poisonous. With the help of Kimball he received permission to do the study in neighboring Akron, Ohio. The treatment group of girls received 200-400 mg NaI per school day for 10 d. The treatment was clearly effective and Marine and Kimball concluded goiter: "...is as easily prevented in man as in fish or in domestic animals".

Based on these studies, general prophylaxis with iodized salt was introduced in the state of Michigan in 1924. There were protests, and at first the Bureau of Chemistry of the Department of Agriculture demanded the iodized salt packages be marked with the skull and crossbones used to indicate a poison, but then backed down. In 1948, the U.S. Endemic Goiter Committee tried to introduce iodized salt to all the states by federal law, but the bill failed.

### The modern era: 1930 to the present

In 1980, the first global estimate from WHO on the prevalence of goiter was reported: it estimated 20–60% of the world's population was iodine deficient and/or goitrous, with most of the burden

in developing countries. But although it was recognized many countries were affected by goiter, little attention was paid to iodine deficiency in public health programs. Goiter was considered a lump in the neck primarily of cosmetic concern; it generated little political attention or action and few resources were allocated for its control.

This changed during the period of 1970–90. Controlled studies in iodine-deficient regions showed that iodine supplementation not only eliminated the incidence of cretinism but also improved cognitive function in the remaining population. Iodine deficiency was thus shown to have social and economic consequences far greater than previously appreciated, that

could slow country development. This changing view allowed iodine deficiency and goiter to be repositioned in the development perspective. The term 'the iodine deficiency disorders (IDD)' was coined, and IDD was repositioned as a spectrum of related disorders affecting 1.5 billion individuals. Programs against IDD had obvious political appeal because its human, economic and social consequences could be averted by a low-cost intervention, universal salt iodization. Since 1990, elimination of IDD has been an integral part of many national nutrition strategies.

# Progress towards elimination of IDD in Kosovo

**Tahire Maloku-Gjergji** National Institute of Public Health, Prishtina, Kosovo; **Ilirjana Zymberaj** Chief Sanitary Inspector of Kosovo, Prishtina, Kosovo; **Agron Gashi** UNICEF, Prishtina, Kosovo; and **Frits van der Haar** ICCIDD



Kosovo is a small landlocked territory of 10,908 km<sup>2</sup> in the center of the Balkan Peninsula with a population of ≈2.1 million. Kosovo is divided into six regions and 30 municipalities. The capital city is Prishtina. Iodine deficiency has been historically

present, with especially high goitre rates in Western Kosovo (Deçan, Peja, Gjakova and Prizren), ranging from 30 to 60%. All salt is imported in Kosovo.

A representative Micronutrient Status Survey conducted in 2001 in Kosovo revealed that 84% of households were using iodized salt and thyroid was palpable in 3% of women of which 0.2% had visible goitre. Half (51%) of the women and school-age children studied had low values (below 100 µg/l) of urinary iodine concentration. Based on these results, Kosovo institutions decided to step up the strategic approaches to address IDD and more vigorously monitor the imports of salt for adequate iodine content.

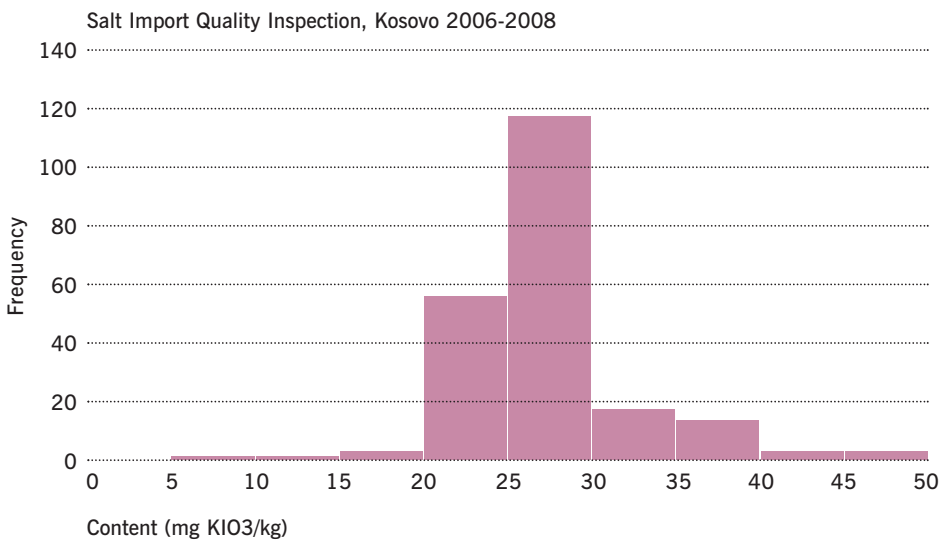
The main means of coordination of the national IDD programme is the working group for IDD and other micronutrient deficiencies, a multi-sector group consisting

of health officials, public health experts, clinicians, sanitary inspectors, laboratory technicians, media, salt importers, flour millers, veterinary inspectors, WHO and UNICEF. The Ministry of Health has recently endorsed an Administrative Instruction for mandatory quality of salt, stipulating the requirement of 30 – 40 mg KIO<sub>3</sub> per kg salt at import.

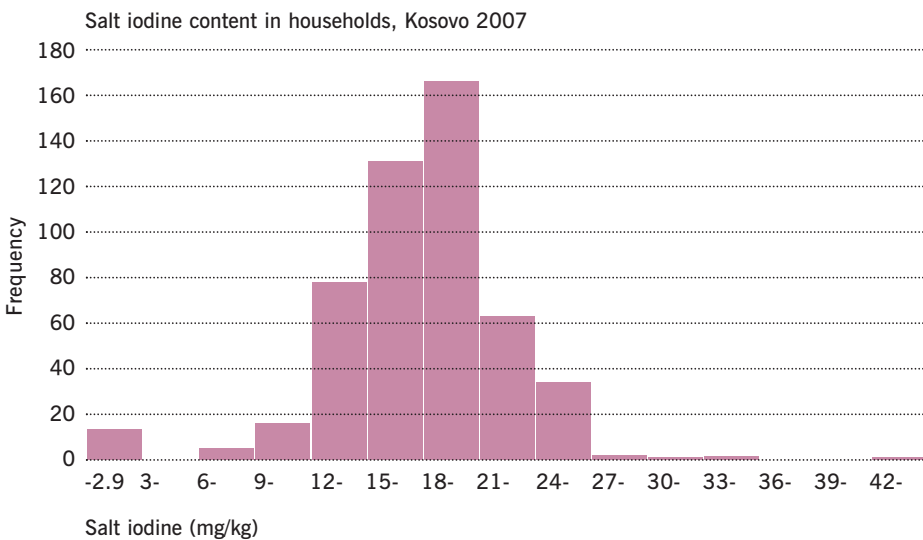
All salt shipments that enter in Kosovo are checked at the border points prior to the release of the shipment. Testing of salt is performed periodically at wholesale and retail points. The National Institute of Public Health in Prishtina and the Institute of Agriculture in Peja have established laboratories for salt quality monitoring. The distribution of iodine content (routinely reported in mg KIO<sub>3</sub>/kg salt) for the 210 salt shipments inspected during 2006, 2007 and January–April 2008 is shown in Figure 1.



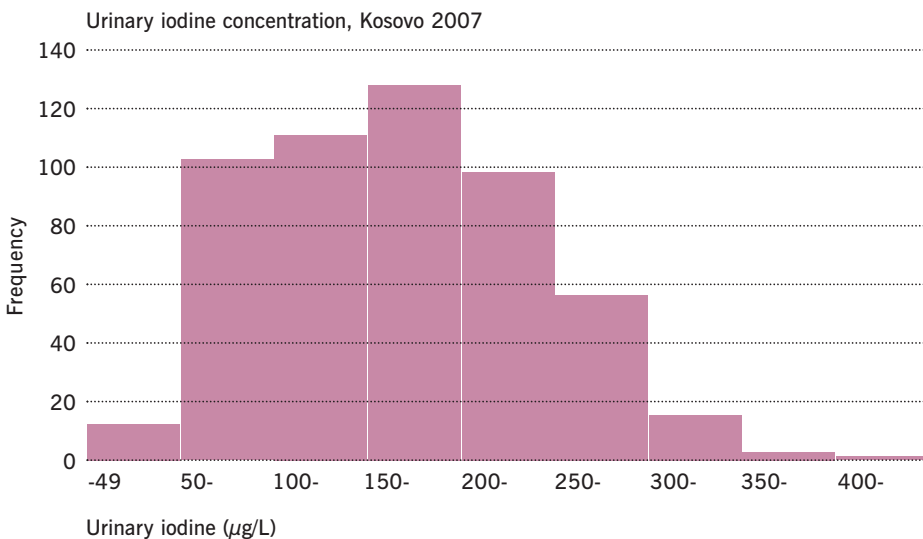
**Figure 1: Salt inspection results of 210 import shipments into Kosovo, 2006-2008**



**Figure 2: Histogram of salt iodine content in 500 household salt samples, Kosovo 2007**



**Figure 3: Histogram of urinary iodine concentration among 521 2nd grade school children, Kosovo 2007**



During this 28-month period, 9 inspections showed too low or high iodine levels (4.3%) and the salt shipments were re-directed to purposes other than consumption. Figure 1 shows that at import, salt for human consumption purposes in Kosovo is iodized at 27 mg KIO<sub>3</sub> per kg salt (16.0 mg iodine/kg), with 95% of the salt ranging between 20.3 and 39.0 mg KIO<sub>3</sub> per kg salt (12.0 – 23.1 mg iodine/kg).



*Iodized salt helps these Kosovar children learn well at school*

The salt monitoring effort is supported by social mobilization activities using all communication channels. During 2007, UNICEF supported the National Institute of Public Health (NIPH) in conducting a national survey to assess biological iodine status (urinary iodine) of school children and the use of iodized salt in households. The survey covered 523 children of the 2nd grade in primary school in rural and urban areas of each region.

The salt iodine results showed 2% of households used non-iodized salt, and that 79% of the salt in households was adequately iodized ( $\geq 15$  mg/kg). The iodine content was 8 – 26 mg/kg in 95% of all the household salt samples (Figure 2) and the median UI of the children was 161 µg/L. Of all children, 22% had UI < 100 µg/L and 95% of the UI values ranged between 51 and 315 µg/L (Figure 3).

Thus, the survey results indicate optimum iodine nutrition status in the population, and indicate acceptable current performance of the national strategies vis-à-vis the mandated salt iodization regulations in Kosovo. An external expert assessment of the progress toward the goal of IDD elimination suggests that Kosovo is meeting international standards. The Ministry of Health and partners are considering proceeding with an application for international recognition.

# Iodine biofortification of plants: an 'alternative' to iodized salt?

A low dose of iodine can stimulate the growth of plants. Small doses may also enhance the antioxidant content – a favorable effect for both crops and consumers. But there is another reason for the growing interest in plant iodine nutrition: food biofortification to control iodine deficiency. Biofortification of staple food crops with micronutrients by either breeding for higher uptake efficiency or fertilization can be an effective strategy to address widespread dietary deficiency in human populations. But is iodine biofortification realistic? Expert views on this potential 'alternative' to iodized salt differ greatly. The following article summarizes recent discussion in this area.

## The pros and cons of iodine in plant nutrition.

G.C. van den Berg *Beneficial Nutrients News* 4:3:August 2008

Iodine stimulates crop growth. A small dose of this nutrient improves the assimilation of nitrogen from fertilizers. In this way, iodine nutrition increases crop yields, fertilizer specialist Kari Jokinen from Kemira GrowHow in Finland concludes from experiments with oilseed rape, ryegrass and wheat. Jokinen discloses this finding in a recently published patent application. If nitrogen stays for a shorter time in the soil, the nutrient is less prone to leaching, volatilization or denitrification. The addition of iodine is especially beneficial to fertilizers high in nitrogen, the Finnish fertilizer specialist says. In his field experiments with arable crops and grass he tested granular fertilizer compositions containing 50 ppm iodine. Besides iodine, the experimental fertilizer compositions of Jokinen also contain traces of selenium. From the experiments with oilseed rape, ryegrass and wheat, he concludes that iodine and selenium enhance crop growth in a synergistic way. At the moment nothing is known about an eventual commercialization of these experimental fertilizer formulations.

Iodine too may stimulate the plants' antioxidant defense system. Proof of an iodine-induced enhancement of the antioxidant level in plants comes from the Spanish plant nutrition specialist Begoña Blasco.

Recently she examined the effects of iodine nutrition on hydroponically grown lettuce in an experimental greenhouse of the Laboratory of Plant Nutrition, at the University of Granada. The treated plants showed a significant increase in antioxidant compounds after the application of iodine. This research however doesn't give insight in the possible growth or yield effects of the enhanced antioxidant level. Examination of the antioxidant status of iodine-fed lettuce was a part of the iodine biofortification project. The most appropriate application rate in hydroponic lettuce cultivation was 40  $\mu\text{M}$ , Begoña Blasco concludes. In spite of a significant iodine accumulation in the leaves, this concentration didn't reduce the biomass of the treated plants.

Although iodine nutrition is also the subject of other patent applications, up until now, iodine has not been recognized as an essential plant nutrient. Even a possibly beneficial status of this element is controversial to many plant nutrition specialists. Some studies show stimulating effects of iodine as plant nutrient, while many other experiments demonstrate harmful effects, illustrated by the herbicidal and defoliant properties of iodide. Iodine too is used as biocide. According to Japanese researchers

an iodine-releasing resin is highly effective in the control of a bacterial disease. This iodinated anion exchange resin is also considered to be suitable for iodine fortification of crops.

Nearly two dozen Chinese patent applications from scientists at Zhejiang University relate to the culture or planting methods of iodine-rich crops and the production of iodine-rich food. The boost in iodine nutrition-related patent publications reflects the increasing interest in iodine biofortification. Huanxin Weng of Zhejiang University primarily examines iodine nutrition for the sake of biofortification of arable and vegetable crops. In the most remote regions of China, he suggests that salt fortification with iodine may not be enough to eliminate iodine deficiency disorders. Weng's work has led to a series of Chinese and international publications on topics ranging from iodine-enriched amaranth to iodine-fortified vigna. At the Research Center for Ecoenvironmental Sciences, Yongguan Zhu studies the prospects of iodine fortification of edible parts of plants. He argues that spinach is particularly suited for iodine fortification.

## Biofortification of crops with seven mineral elements often lacking in human diets – iron, zinc, copper, calcium, magnesium, selenium and iodine.

Philip White and Martin Broadley *New Phytologist* 2009;182(1):49-84

These plant biologists from universities in the United Kingdom discuss the potential of iodine fortification of plants through several means, including iodine-containing fertilizers. In most soils, iodine is present in solution as iodide, although iodate can also be present under strongly oxidizing conditions. Fertilization with soluble iodide and/or iodate salts has been practised in

agriculture, and the iodination of irrigation water has successfully increased the delivery of iodine to humans through edible crops. The iodine concentrations in root crops and leafy vegetables can be increased greatly by the application of iodine fertilizers, and, although iodine is not readily mobile in the phloem, iodine concentrations in tubers, fruits and seeds

can also be increased by iodine fertilization to nutritionally significant concentrations. It has been even suggested that, because human dietary iodine requirements are quite low, iodine fertilizers might be added to large areas of agricultural production from aeroplanes.

## Exploiting micronutrient interaction to optimize biofortification programs: The case for inclusion of selenium and iodine in the HarvestPlus program.

GH Lyons, JC Stangoulis, RD Graham *Nutrition Reviews*. 2004;6:247-252

These scientists from the University of Adelaide in Australia argue that iodine should be included in the HarvestPlus program. HarvestPlus is a CGIAR global challenge program seeking to reduce micronutrient malnutrition by breeding staple food crops that are rich in micronutrients through biofortification. More research is needed to determine whether sufficient genetic variability exists within staple crops to enable selection for iodine uptake efficiency. Selenium and iodine deficiencies affect a large proportion of the population in countries targeted for biofortification of staple crops with zinc, iron, and vitamin A, and inclusion of selenium and iodine would be likely to enhance the success of these programs. Interactions between selenium and iodine in the thyroid gland are



well established. Moreover, selenium appears to have a normalizing effect on certain nutrients in the body. For example, it

increases the concentration of zinc and iron at key sites such as erythrocytes when these elements are deficient, and reduces potentially harmful high Fe concentration in the liver during infection. An important mechanism in selenium /zinc interaction is selenoenzyme regulation of zinc delivery from metallothionein to zinc enzymes. Whether sufficient genetic variability exists within staple crops to enable selection for selenium uptake efficiency remains to be demonstrated. In addition, bioavailability trials with animals and humans are needed, using varying dietary concentrations of selenium, iodine, zinc, iron, and vitamin A to elucidate important interactions in order to optimize delivery in biofortification programs.

## Further reading

Iodine in soil-plant systems and prevention of iodine deficiency disorders. *Ecology and Environment* 2003;2:228-231

Effects of iodine on growth and iodine absorption of hydroponically grown tomato and spinach. *Horticultural Research (Japan)* 2007;2:223-227

Effect of iodine treatments on forage yields of alfalfa. *Communications in Soil Science and Plant Analysis*. 2003;1-2:55-64.

Increment of iodine content in vegetable plants by applying iodized fertilizer and the residual characteristics of iodine in soil. *Biological Trace Element Research*. 2008;1-3:218-228

Iodine biofortification and antioxidant capacity of lettuce: potential benefits for cultivation and human health. *Annals of Applied Biology* 2008;3:289-299

Availability of iodide and iodate to spinach (*Spinacia oleracea* L.) in relation to total iodine in soil solution. *Plant and Soil* 2006;1-2:301-308



# Meetings and Announcements

## Annual Meeting of the Institute of Food Technologists, June 8, 2009, Anaheim, CA, USA

David Haxton, ICCIDD Executive Director and Dick Hanneman, ICCIDD Board Member, are co-chairing a session on June 8, 2009 at the Annual Meeting of the Institute of Food Technologists in Anaheim, CA, USA. There will be a panel discussing use of iodized salt in processed foods; the five-person panel includes three ICCIDD board members (Venkatesh Mannar, Gregory Gerasimov and Kevin Sullivan); the other two are from the salt industry (Wally Becky of Morton Salt and Yang Haiyan of China Salt).

## Salt Symposium, September 4-6, 2009, Beijing, China

The 2009 Salt Symposium will take place September 4-6, 2009 in Beijing, China. The Symposium is held every eight or nine years. The last one took place in The Hague, The Netherlands in 2000, and gave birth to the Global Network for the Sustained Elimination of IDD. China Salt, a Network board member, is the organizer of the Symposium. IDD elimination is one of the main themes of the Symposium and there will also be a Round Table which aims to reinvigorate the salt industry and to mobilize a new generation of salt leaders for universal salt iodization (USI).

ICCIDD, the Network and UNICEF plan to make the Beijing Symposium a major advocacy event on USI/IDD elimination. High level participation from the Chinese government, UNICEF and various IDD stakeholders is expected.

## Abstracts

### Methods of assessment of iodine status in humans: a systematic review.

The authors performed a structured search for iodine intervention studies and a random-effects meta-analysis was performed. Twenty-one intervention studies were included. Urinary iodine (in children and adolescents and in those with low and moderate baseline iodine status), thyroglobulin (in children and adolescents but not in pregnant and lactating women), serum thyroxine (in children and adolescents, adults, women, and those with moderate baseline thyroxine status but not in pregnant and lactating women), and serum thyroid-stimulating hormone (in pregnant and lactating women but not in children

and adolescents or those at moderate baseline status), but not triiodothyronine, proved to be useful biomarkers of iodine status.

*Ristic-Medic D et al. Am J Clin Nutr. 2009 May 6. [Epub]*

### Thyroid volume changes during pregnancy and after delivery in an iodine-sufficient Republic of Slovenia.

The authors prospectively studied healthy pregnant women living in an iodine-sufficient area. 118 pregnant women were studied in the first trimester, in the third trimester and 4 and 14 months after delivery. All women were negative for thyroid autoantibodies. Median UIC in the third

trimester (176 µg/g creatinine) was significantly higher than 4 and 14 months after delivery. Mean thyroid volume in the third trimester (11.3 mL) was significantly greater than in the first trimester (8.7 mL), 4 months after delivery (8.6 mL) and 14 months after delivery (7.8 mL). TSH concentration was significantly higher in the third trimester than in the first trimester and 4 months after delivery. In an iodine-sufficient area, thyroid volume increases during pregnancy but then decreases back to prepregnancy size after delivery.

*Fister P et al. Eur J Obstet Gynecol Reprod Biol. 2009 Apr 28. [Epub]*

### **Iodine concentration of milk in a dose-response study with dairy cows and implications for consumer iodine intake.**

Most feed is poor in iodine and iodine supplementation of cow's diets must guarantee milk iodine concentrations for humans that contribute to prevention of the deficiency and minimize the risk of exceeding an upper limit of iodine intake. Holstein cows were fed four iodine doses in four sequential 14-d periods, doses of 0.2 (basal diet), 1.3, 5.1, and 10.1 mg iodine/kg diet dry matter (DM) were administered. Samples of milk were collected during each period. The mean levels for the four doses tested in milk were 101, 343, 1215, and 2762 µg/kg. The iodine supplementation of 0.5-1.5 mg/kg diet DM represents the requirement of the cow, resulting in 100-300 µg/L milk, which optimally contributes to human supply. The maximum dietary levels of former and present EU legislations (10 and 5 mg iodine/kg cow feed) increase the risk of iodine excess in humans.

*Schöne F et al. J Trace Elem Med Biol. 2009;23(2):84-92.*

### **Association of iodine fortification with incident use of anti-thyroid medication - A Danish nationwide study.**

The objective of this study was to monitor the effect of the Danish iodine fortification program on incidence of hyperthyroidism as measured by the incident use of anti-thyroid medication. In the region with previous moderate iodine deficiency the number of incident users of anti-thyroid medication increased 46% in the first four years of iodine fortification. In the previously mildly iodine-deficient region the number of incident users increased only 18%. After four years of fortification the incidence rates started to fall and reached baseline, for most groups, six years after onset of fortification. This study

shows that iodine fortification induced a temporary, modest increase in the incidence of hyperthyroidism as measured by use of anti-thyroid medication.

*Cerqueira C et al. J Clin Endocrinol Metab. 2009 Apr 14. [Epub]*

### **Delayed neurobehavioral development in children born to pregnant women with mild hypothyroxinemia during the first month of gestation: the importance of early iodine supplementation.**

The authors evaluated the neurocognitive performance at 18 months of age in three groups of children: group 1 included children of women with free thyroxine >20th percentile at 4-6 gestational weeks and at full-term. Group 2 included children of mildly hypothyroxinemic women diagnosed during the first 12-14 weeks and with FT(4) >20th percentile at full-term.

Women were iodine supplemented from the day of enrollment until the end of lactation. Group 3 included children born to mildly hypothyroxinemic women at full-term, without iodine supplementation during gestation. The data suggested a delay of 6-10 weeks in iodine supplementation (200 µg KI/d) of hypothyroxinemic mothers at the beginning of gestation increases the risk of neurodevelopmental delay in the progeny.

*Berbel P et al. Thyroid. 2009;19(5):511-9.*

### **Using bread as a vehicle to improve the iodine status of New Zealand children.**

The authors determined the iodine status in 93 New Zealand school children, and estimated how the addition of iodized salt to bread will improve their iodine status. Iodine status was assessed by urinary iodine concentration (UIC), serum thyroglobulin (Tg), and dietary iodine intake was estimated using an iodine-specific food frequency questionnaire. It was estimated that the addition of iodized salt to bread

would increase the average iodine intake of these children to 75-104 µg/day, decrease the number of children who have an iodine intake less than the EAR to 4-46% and increase the median UIC of these children to 95-151 µg/L. Thus, the introduction of iodized salt to bread, which is currently scheduled to become mandatory in September 2009, should improve the iodine status of New Zealand children.

*Rose M et al. N Z Med J. 2009;122(1290):14-23.*

### **Requesting iodine supplementation in children on parenteral nutrition.**

Iodine supplementation of parenterally fed infants is recommended at 1 µg/kg/day. Children (1-17 yrs; n=15), undergoing parenteral nutrition (PN) and receiving an iodine supply of 1 µg/kg/day, were enrolled. They were on PN from 14 to 84 weeks; nine had short bowel syndrome (SBS) and six had other intestinal diseases requiring PN. The authors found an inverse correlation between duration of PN in months and urinary iodine concentration (UIC). After 12 weeks, 53% of patients had UIC<50 µg/L, but thyroxine, TSH and thyroid volume remained unchanged. Thus, a PN iodine supply of 1µg/kg/day may be suboptimal in PN.

*Cicalese MP et al. Clin Nutr. 2009 Mar 6. [Epub]*

**Thyroid function in early pregnancy in Japanese healthy women: relation to urinary iodine excretion, emesis, and fetal and child development.**

The objective of the study was to examine urinary iodine excretion and thyroid function in early pregnancy in Japanese healthy women (n=662), and fetal maturation and child development in these women. The distribution of urinary iodine concentrations was large, and the average was extremely high. There were significant positive correlations between urinary iodine and serum TSH ( $r = 0.1326$ ;  $P < 0.005$ ), but iodine excess during early pregnancy had no measurable adverse effects on the fetus.

*Orito Y et al. J Clin Endocrinol Metab. 2009;94(5):1683-8.*

**Association of high iodine intake with the T1799A BRAF mutation in papillary thyroid cancer.**

Epidemiological studies have indicated that high iodine intake might be a risk factor for papillary thyroid cancer (PTC), which commonly harbors the oncogenic T1799A BRAF mutation. The objective of the study was to investigate the relationship between BRAF mutation in PTC and iodine intake in patients (n=1032) from five regions in China that harbor different iodine contents in natural drinking water, ranging from normal (10-21 µg/L) to high (104-287 µg/L). The prevalence of BRAF mutation was significantly higher in the regions with high iodine content than any of the regions with normal iodine content.

*Guan H et al. J Clin Endocrinol Metab. 2009;94(5):1612-7.*

**Iodine levels and thyroid hormones in healthy pregnant women and birth weight of their offspring.**

The study assessed the association between thyroid hormones (THs) and urinary iodine concentration (UIC) in healthy pregnant women (n=657) and the birth weight of their children. Six percent of newborns were classified as small for gestational age (SGA). Women with the third trimester UICs between 100 and 149 µg/L had lower risk of having an SGA newborn than women with UICs below 50 µg/L (adjusted OR (95%CI): 0.15 (0.03-0.76)). There was no significant reduction in SGA among mothers with higher UICs. Thus, iodine status during pregnancy may be related to prenatal growth in healthy women.

*Alvarez-Pedrerol M et al. Eur J Endocrinol. 2009 Mar;160(3):423-9.*

THE IDD NEWSLETTER is published quarterly by ICCIDD and distributed free of charge in bulk by international agencies and by individual mailing. The Newsletter is also distributed to email subscribers and appears on ICCIDD's website ([www.iccidd.org](http://www.iccidd.org)). The Newsletter welcomes comments, new information, and relevant manuscripts on all aspects of iodine nutrition, as well as human interest stories on IDD elimination in countries.

For further details about the IDD Newsletter, please contact:

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