JOD

Quack Lötscher, K C

Abstract: Report written by a group of experts on behalf o the Federal Commission for Nutrition (FCN) 2012. Approved the by Federal Commission for Nutrition on February 10, 2013.

Other titles: Iodine supply in Switzerland: Current status and recommendations

Iodine supply in Switzerland:

Current Status and Recommendations

Report written by a group of experts on behalf of the Federal Commission for Nutrition (FCN) 2012

Approved by the Federal Commission for Nutrition on February 10, 2013.

© and correspondence:
Federal Office of Public Health,
Division of Food Safety, Nutritional and Toxicological Risks Section
Stauffacherstrasse 101
8004 Zurich
Tel. 043 322 21 96, Fax: 043 322 21 99

Citation:
Federal Commission for Nutrition. Iodine supply in Switzerland: Current Status and Recommendations. Expert report of the FCN. Zurich: Federal Office of Public Health, 2013.

Table of contents

Foreword

Prof. Dr.med. Ulrich Keller
President of the Federal Commission for Nutrition (FCN)

Switzerland is an iodine deficient area, and iodine has been added to table salt since 1922.

To ensure sufficient iodine intake in Switzerland, iodine supply is continuously monitored at 5 year intervals since 1999. Iodine supply is surveyed by the Iodine-Fluoride Committee of the Swiss Academy of Medical Sciences, formerly the Swiss Commission on Goiter.

Based on the monitoring, the amount of iodine that is added to table salt can be adjusted if needed.

The importance of this strategy has increased due to the changing eating habits of today's society, with more and more meals consumed out of home, and due to the internationalization of the food market. Imported convenience foods or domestic cheese may have been prepared with non-iodinated salt, and the current trend to reduce salt consumption by adding less salt e.g. to bread further endanger sufficient iodine supply for the population.

The last monitoring was performed in 2009 and it appears that an increasing part of high risk groups (pregnant and lactating women, young children) are at risk to be iodine deficient. Therefore, the Federal Commission on Nutrition asked the Federal Office of Public Health to support the production and publication of an expert report on iodine supply in Switzerland.

This report has now been completed, and it has been ratified by the members of the FCN.

We would like to thank the authors, and in particular the president of the working group, Prof. Michael Zimmermann, ETH Zurich, for their outstanding contributions.

This report should provide the background for an adjustment of iodine supplementation of Swiss table salt, and it should provide valuable informations for the food industry, for people teaching human nutrition and for public health experts. Last but not least, it should improve iodine supply particularly to persons with increased risk of inadequate provision, thereby preventing adverse effects of iodine deficiency.

Authors of the chapters

Executive Summary:
Prof. Dr. med. Michael Zimmermann
Human Nutrition Laboratory, ETH Zürich
Schmelzbergstrasse 7, LFV E19, 8092 Zürich
michael.zimmermann@hest.ethz.ch

Chapter 1:
Dr. med. Katharina C. Quack Lötscher MPH
Department of Obstetrics and Gynaecology
University Hospital, Zurich, 8091 Switzerland
Katharina.QuackLoetscher@usz.ch

Chapter 2:
Prof. Dr. med. Michael Zimmermann
Human Nutrition Laboratory, ETH Zürich
Schmelzbergstrasse 7, LFV E19, 8092 Zürich
michael.zimmermann@hest.ethz.ch

Chapter 3:
Prof. Dr. med. Hans Bürgi[1] and Dr. Maria Andersson[2]

[1] Human Nutrition Laboratory, ETH Zürich
Schmelzbergstrasse 7, LFVE19, 8092 Zürich
maria.andersson@hest.ethz.ch

[2] Verenaweg 26, 4500 Solothurn
hans.buergi@gmail.com

Chapter 4:
Max Haldimann[1] and Dr. Elizabeth Stalder[2]

[1] Bundesamt für Gesundheit
Abteilung Lebensmittelsicherheit, Sektion Chemische Risiken
Schwarzenburgstrasse 165, 3003 Bern
max.haldimann@bag.admin.ch

[2] Bundesamt für Gesundheit
Abteilung Lebensmittelsicherheit, Sektion Chemische Risiken
Schwarzenburgstrasse 165, 3003 Bern
lizstalder@swissonline.ch

Chapter 5:
Dr. Maria Andersson
Human Nutrition Laboratory, ETH Zürich
Schmelzbergstrasse 7, LFVE19, 8092 Zürich
maria.andersson@hest.ethz.ch

Members of the working group

- Prof. Dr. med. Michael Zimmermann (president of the working group)
  Human Nutrition Laboratory, ETH Zürich
  Schmelzbergstrasse 7, LFV E19, 8092 Zürich.
  Tel: +41 44 632 86 57, Fax: +41 44 631 14 70
  michael.zimmermann@hest.ethz.ch

- Prof. Dr. med. Hans Bürgi (member)
  Verenaweg 26, 4500 Solothurn.
  Tel: +41 32 622 03 02, Fax: +41 32 621 24 35
  hans.buergi@gmail.com

- Dr. Maria Andersson (member)
  Human Nutrition Laboratory, ETH Zürich
  Schmelzbergstrasse 7, LFVE19, 8092 Zürich
  Tel: +41 44 632 8051, Fax: +41 44 632 1470
  maria.andersson@hest.ethz.ch

- Prof. Dr. med. Christoph A. Meier (member)
  Departement für Innere Medizin, Stadtspital Triemli
  Birmensdorferstr. 497, 8063 Zürich
  Tel: +41 44 466 21 01 , Fax: +41 44 466 26 02
  christoph.meier@triemli.stzh.ch

Executive Summary

Prof. Dr.med. Michael B. Zimmermann
President of the Iodine/Fluoride Committee of the Swiss Academy of Medicine

Historically, Switzerland was a country of severe endemic goiter and cretinism. In 1922, Eggenberger, chief surgeon at the hospital in Herisau, introduced iodized salt into the Canton of Appenzell Ausserrhoden. Within one year, goiter size was sharply reduced in affected children. Recognizing the enormous public health benefit, the United Swiss Rhine Salt Works began to produce iodized salt and the Swiss Federal Office of Public Health formed the Swiss Goiter Commission in 1922. This Commission proceeded cautiously with iodine fortification, raising the iodine content of Swiss salt in four steps over a period of 90 years, from 3.75 ppm to the current level of 20 ppm. The goiter rate in school-age children is now below 5% and no new cretins have been born since 1930. In 2012, the Swiss iodized salt program remains a model for many other countries. **Chapter 3** of this report briefly summarizes the history of Swiss iodine prophylaxis.

Iodine is essential for normal growth and development because it is an essential component of the thyroid hormones. Because thyroid hormones regulate normal fetal growth and brain development, *in utero* iodine deficiency can irreversibly damage the offspring. Thus, it is critical to provide ample dietary iodine during pregnancy (requirements are 250 µg/day), a 50% increase compared to pre-pregnancy (150 µg/day). Infants are born with very limited thyroidal iodine stores and are dependent on a steady supply of dietary iodine. Breast milk or infant formula should provide at least 90 µg of iodine per day to cover infant requirements. Breastfed infants of iodine sufficient mothers obtain adequate iodine from breast milk and do not need supplemental sources of iodine. Because dairy products and iodized salt are the major sources of iodine in the Swiss diet, weaning infants fed only complementary foods without added salt are at risk of iodine deficiency. Once the infant has weaned from breast milk and is beginning to eat other foods, provision of iodine-fortified complementary foods, follow-on formula containing iodine and/or home-prepared foods containing iodized salt, may be important to meet their iodine requirements. Mild-to-moderate iodine deficiency during later childhood can impair cognitive function and learning, and recent controlled trials of iodine repletion in school-aged children have shown benefits on cognitive and motor test performance. Thus, pregnant and lactating women, infants and children are important target groups for iodine prophylaxis in the Swiss population. **Chapters 1 and 2** of this report describe the effects of iodine deficiency on pregnant and lactating women, as well as infants and children.

In Switzerland, the Federal Office of Public Health measures the content of iodine in food groups to identify and quantify major sources of dietary iodine in the population. Nearly all foods, with the exception of marine fish, contain very low amounts of iodine. Milk and milk products are important sources of iodine in the Swiss diet, because iodine is introduced via supplements given to dairy cows (particularly in winter). The other main sources of iodine in the Swiss diet are bread and baked goods, because many bakeries voluntarily use iodized salt. The iodine concentration in other foodstuffs, such

as meat, vegetables and fruits, is extremely low. Cheese could be an important source of iodine in Switzerland, because of the iodine content of milk and iodized salt added during production. Yet most Swiss cheese producers have discontinued the use of iodized salt for two main reasons: 1) the inability to export products to France containing added iodine; and 2) the new Swiss 'Deklarationspflicht' that specifies that cheese containing iodized salt must have an ingredient label, whereas cheese containing non-iodized salt need not have a label of ingredients.

Use of iodized salt by Swiss households remains high, at greater than 80%, but use of iodized salt in industrially processed foods may be decreasing. In Switzerland, iodized salt consumed from home-cooked food contributes only a small proportion of the total iodine intake since most salt consumption is from processed foods. Thus, use of iodized salt by the food industry is critical and must be strongly promoted. Therefore, when considering changes to the iodine content of Swiss salt to increase dietary iodine intake in the population, the focus should be on the food industry rather than only household salt. The Swiss Federal Office of Public Health estimates an adult following the dietary recommendations of the Swiss Society for Nutrition will have a mean iodine intake of approximately 145 µg/day, near the adult requirement of 150 µg/day. However, people following restrictive eating behaviors, such as a strict vegan diet without milk or eggs, may be at risk of iodine deficiency, particularly if they do not use iodized salt. Nutritional habits, food formulation and production procedures are constantly changing, and since all of these factors can influence iodine intakes, regular monitoring of iodine nutrition in Switzerland will remain important. **Chapter 4** of this report summarizes the iodine content of Swiss foods and iodine sources in the Swiss diet.

In Switzerland, iodine status in target groups is monitored every 5 years through national surveys. The main indicator used in these surveys is the urinary iodine concentration (UIC), an excellent biomarker of population exposure because most dietary iodine is excreted in the urine in the following 24 hours. In the last two national surveys, in 2004 and 2009, the median UIC in school-age children and pregnant women indicated sufficient iodine intake. However, iodine intakes fell in these groups between 2004 and 2009. In addition, in 2009, infants, lactating women and women of reproductive age had borderline low iodine intakes. Thus, although Switzerland is still considered an iodine sufficient country, iodine intakes appear to be decreasing in key target groups, and are currently at the lower end of the recommended range in pregnant women and children. These monitoring data suggest a modest increase in the iodine content of Swiss salt is needed in order to ensure iodine sufficiency in all population groups. **Chapter 3** of this report describes the recent epidemiology of iodine nutrition in Switzerland.

Current efforts to lower population sodium intake in Switzerland to reduce hypertension do not conflict with the salt iodization program; these two important public health policies can be complementary but public health messages need to be integrated to avoid confusion. Future reductions in salt intake will require adaptations to the Swiss iodized salt program by: 1) ensuring high penetration rate of iodized salt in food production; and 2) adjusting iodine fortification levels in salt upward to compensate for lower salt intake. Regular monitoring of iodine status should continue in school age children, pregnant women and infants. For the latter two groups, if the iodized salt program cannot provide adequate iodine intakes, alternative intervention strategies will need to be considered. An effective iodized salt

program in Switzerland requires a joint effort of all partners including the Swiss Federal Office of Public Health, salt industry, food producers, academia, health professionals and consumer organizations. **Chapter 5** in this report summarizes the critical role of the food industry, partnerships and integration of iodized salt and sodium reduction programs.

Conclusions and Recommendations

1. The long-running Swiss iodized salt program, a model for most other countries, has provided adequate iodine to the population for decades. But it is critical not to become complacent.

2. Sponsored by the Swiss Federal Office of Public Health, the ETH Zurich performs national iodine surveys every 5 years since 1999. In the last two surveys, in 2004 and 2009, the median urinary iodine concentration in school-age children and pregnant women indicated sufficient iodine intake. However, iodine intakes fell in these groups between 2004 and 2009, and are currently at the lower end of the recommended range. In the 2009 survey, infants, lactating women and women of reproductive age had borderline low iodine intakes (Chapter 3 of this report). Thus, at the current fortification level of 20 ppm iodine in salt in Switzerland, iodine intakes are borderline sufficient. To ensure iodine sufficiency in all population groups, it would be prudent to increase the iodine concentration in Swiss salt to 25 ppm in 2013.

3. The current median UICs in school children and pregnant women in Switzerland are 120 µg/L and 162 µg/L. These medians are far below the WHO-recommended thresholds for excessive iodine intake based on the median UIC in these two groups of 300 µg/L and 500 µg/L, repectively. Also, the percentage of Swiss school children with a UIC above the UL of 300 µg/day is <1%. Thus, the current iodized salt program is not placing the Swiss population at risk for iodine excess. If the iodine content in Swiss salt were to increase ca. 20% (i.e. if the iodine level is increased from 20 to 25 ppm in 2013), there would still be very low risk of iodine excess. WHO/ICCIDD currently recommend to set salt iodization levels in national programs in the range of 20 to 40 ppm (18), and the Swiss fortification level is at the lower end of this recommended range.

4. Because overall, Swiss pregnant women are iodine sufficient, routine iodine supplementation during pregnancy is not needed for healthy women eating typical Swiss diets. But for those Swiss pregnant women who may have low iodine intakes because they do not use iodized salt, a prenatal supplement containing 150-200 µg iodine per day is advisable. Most prenatal supplements available in Switzerland do not contain iodine. Supplement manufacturers should be encouraged to include iodine in their prenatal products so that pregnant women with diets low in iodine can obtain adequate iodine intake. Swiss pregnant women who are consuming iodized salt can also safely consume a prenatal iodine supplement containing 150-200 µg iodine per day.

5. Breast milk is the most important iodine source during infancy and lactating women should be advised to consume iodized salt and choose foods produced with iodized salt. Breastfed infants of iodine sufficient mothers obtain adequate iodine from breast milk and do not need supplemental sources of iodine. Once the infant has weaned from breast milk and is beginning to eat other foods, provision of iodine-fortified complementary foods, follow-on formula containing iodine and/or home-prepared foods containing iodized salt, may be important to

meet their iodine requirements. In home-prepared infant foods, salt should only be added beginning in the second year and only added in moderation. The salt used should be iodized.

6. Dietary iodine supply in Switzerland is influenced by many hidden factors, use of iodized salt by Swiss households and the food industry is voluntary, and changes in industrial practices and trade legislation can reduce dietary iodine supply. Therefore, regular surveys of iodine status in Switzerland are necessary to ensure adequacy in the face of not-always-predictable changes in salt and food consumption practices. It is essential to continue the national iodine surveys at 5 year intervals, and include functional indicators of thyroid status where appropriate (e.g., serum thyroglobulin, newborn TSH) to ensure coverage the key target groups.

7. Iodized salt consumed from home-cooked food contributes only a small proportion of the total iodine intake since most of salt consumption in Switzerland comes from processed foods. Therefore, it is critical that the Swiss food industry continue to use iodized salt in their products. To achieve this, strong and sustained advocacy toward the food industry from the Swiss government and other concerned groups is important. Also, if required, the Federal Office of Public Health should provide technical training and assistance to the food industry to establish quality control procedures to monitor the use of iodized salt in the food production and analytical procedures to measure iodine content in food.

8. Public health recommendations and dietary guidelines now encourage people to reduce their salt intake for cardiovascular health, and this could have a detrimental effect on iodine intakes of the Swiss population, as fortified salt is the main dietary source of iodine. These two important public health policies can be complementary but it is important they be integrated. Concurrent monitoring of sodium and iodine intakes could be implemented. If salt intakes fall, this will require adaptations to the Swiss iodine program, including: 1) ensuring the highest possible penetration rate of iodized salt in food production; and 2) adjusting the iodine fortification levels in salt to compensate for the lower salt intake.

9. Commercially produced bread is the most important source of dietary iodine in Switzerland. However, bread contains relatively high concentrations of salt and is therefore a target for salt reduction. However, an increase in the salt iodine concentration could compensate for a decrease of the salt content in bread.

10. Future priorities in **research** to inform and optimize the Swiss iodized salt program include:
    a) Accurately assess the extent of iodized salt use in Swiss food production, and incorporate information on the native iodine content and the iodized salt content in Swiss foods into the Swiss Food Composition Database;
    b) Adapt the protocol of the upcoming Swiss National Nutrition Survey to include salt and iodine intake so that the dietary data collected can be used in model analysis to predict changes in salt and iodine intake;
    c) Better define the requirements for iodine in pregnant and lactating women and young infants by using prospective longitudinal studies.

11. Future priorities in the area of **public policy** should include:
    a) Promote use of iodized salt in production of all foods, including its use in business and school cafeterias
    b) Make necessary adjustments to iodine levels in salt based on the population's salt intake patterns;
    c) Ensure adequate iodine intakes in vulnerable groups, i.e. infants, children, pregnant women and lactating women;
    d) Evaluate the need for iodine supplementation of pregnant and lactating women;
    e) Promote the inclusion of iodine in all prenatal supplements to ensure adequate intakes in pregnancy along with intakes from iodized salt (recommendation 4 above)
    f) Evaluate the need to develop a separate policy for iodine fortification of infant formula and complementary foods.

12. Future priorities in **political commitment and legislation** should include:
    a) Support coordinated European efforts to raise the priority of iodine nutrition on the political agenda in Europe and support a common EU policy for the use of iodized salt by the food industry.

13. Future priorities in building **partnership** should include:
    a) Ensure continued participation of government partners, national agencies, nongovernmental organizations, salt producers, academia and the health-care sector in the Swiss Fluoride/Iodine Committee;
    b) Provide support and continue the mandate of the Swiss Fluoride/Iodine Committee to review information from monitoring activities for planning and promotion of collaborative work between the different sectors;
    c) Encourage greater participation of food industry and consumer organizations.

14. Future priorities in **advocacy and communication** should include:
    a) Promote the use of iodized salt in all food production and all households;
    b) Develop appropriate communication through mass media, the health system, food industry organizations, and other context specific channels to educate the public, salt producers and food producers about the importance of iodine nutrition and iodized salt;
    c) Provide support to the Schweizer Rheinsalinen AG to increase the demand for iodized salt from the food industry;
    d) Information campaigns of iodine nutrition should be combined with and integrated into salt reduction campaigns; advocacy should combine messages on the benefits of salt reduction and adequate iodine intake.

Chapters of the Report

1. Iodine in pregnancy, lactation and infancy, and the importance of iodine in weaning foods

Dr. med. Katharina Quack Lötscher

The author declares no conflict of interest.

1.1. Summary

Thyroid hormones are essential for normal fetal brain development and fetal growth. Iodine requirements are 50% higher in pregnant women than in nonpregnant women due to: i) increased maternal thyroid hormone production to maintain maternal euthyroidism; ii) the transfer of thyroid hormones and iodine to the fetus, and; iii) an increased maternal renal iodine clearance. Iodine intakes in pregnant and lactating women should be 250 µg daily. Infants are born with limited intrathyroidal iodine stores and newborns are entirely dependent on dietary iodine. Breast milk or infant formulas should provide at least 90 µg of daily iodine to cover the newborn's needs. Breastfed infants of iodine sufficient mothers obtain adequate iodine from breast milk and do not need supplemental sources of iodine. Because dairy products and iodized salt are the major sources of iodine in the Swiss diet, weaning infants fed only complementary foods without added salt are at risk of iodine deficiency. Once the infant has weaned from breast milk and is beginning to eat other foods, provision of iodine-fortified complementary foods, follow-on formula containing iodine and/or home-prepared foods containing iodized salt, may be important to meet their iodine requirements. In home-prepared infant foods, iodized salt should only be added beginning in the second year and only added in moderation.

1.2. Pregnancy

1.2.1 Iodine and thyroid physiology in pregnancy

Iodine is an essential component of the thyroid hormones thyroxine (T4) and 3,5,3'-triiodothyronine (T3) and gestational iodine requirements increase due to the increased synthesis of thyroid hormones during pregnancy. The rising concentrations of estrogens induce an increase in serum thyroxine-binding globulin (TBG) which reaches a plateau at mid-gestation that lasts until delivery (1) (**Figure 1**). Nuclear receptors for thyroid hormones are only present in the fetal brain after the 9th week of gestation, reaching adult levels by the 18th week of gestation (2). At the end of the first trimester, placental human chorionic gonadotropin (hCG), which has an intrinsic TSH-like activity, stimulates the liver to increase levels of thyroxine-binding proteins, as well as to increase transplacental passage of thyroid hormones and increase iodine excretion by the kidney (3). The binding capacity of TBH for T4 is increased and produces a transient decrease in free T4 concentration, which stimulates further production of T4, thereby leading to a new equilibrium (**Figure 1**). Maternal T3 and T4 levels rise in early pregnancy, reach a plateau and subsequently decline over later pregnancy. Around the beginning of the second trimester the fetal thyroid begins to produce hormones; however, the full

development of the pituitary-thyroid system in the fetus is not completed until mid-pregnancy. Although the T4 concentration in the fetus increases as gestation progresses, the fetal thyroid gland does not fully mature until birth and thus maternal thyroid hormones contribute to total fetal thyroid concentrations until birth (4).

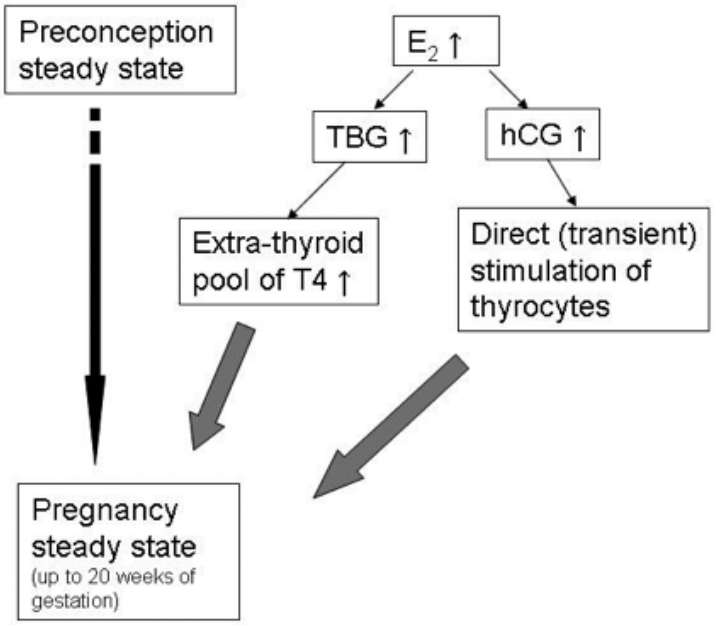

Figure 1: Conceptual model of the changes in hormones that occur during pregnancy that influence iodine requirements. (Adapted from reference (1). E_2, estrogen; hCG, human chorionic gonadotrophin; TBG, thyroxine-binding globulin; T4, thyroxine.

Both thyroid hormones, T3 and T4, play an important role in the normal growth and development of the central nervous system. Despite the placenta acting as a barrier to prevent excessively high levels of free T3 and T4, maternal thyroid hormones can be found in embryonic cavities about four weeks after conception (2, 5). In the first half of pregnancy, maternal thyroid hormones are the only source for fetal cerebral T3, which is generated locally from maternal free T4 in the fetal brain by a type II 5'-iodothyronin deiodinase (4). In the second half of pregnancy, neurodevelopment remains thyroid hormone-dependent and requires an adequate supply of maternal and fetal free T4. This stage includes neuronal proliferation and the onset of neuronal migration in the cerebral cortex, hippocampus and medial ganglionic eminence, with the latter processes starting in the first trimester and continuing into the early part of second trimester (2).

1.2.2 Iodine requirements

To produce sufficient thyroid hormone to meet fetal requirements, maternal iodine intake should increase by 50% to about 250 µg/day during pregnancy (daily requirements are 150 µg/day for nonpregnant women) and the urinary iodine concentration (UIC) should be 150-249 µg/L (13). The increase in requirement is due to: i) a 50% rise in maternal thyroid hormone production up to mid-pregnancy; ii) increased renal blood flow and iodine clearance (30-50%) in the first weeks of gestation; and iii) iodine transfer to the fetus, particularly in late gestation (6, 7). These physiological changes

tend to lower plasma inorganic iodine (PII) and increase thyroidal clearance of iodine. Insufficient dietary intake over an extended period of time may gradually deplete the thyroidal iodine stores (1, 8).

Because >90% of ingested iodine is excreted in the urine, UIC is an excellent indicator of recent iodine intake in all ages (13). UIC can be expressed as a concentration (µg/L), in relationship to creatinine excretion (µg iodine/g creatinine), or as 24-hour excretion (µg/day). For populations, because it is impractical to collect 24-hour samples in field studies, UI can be measured in spot urine specimens from a representative sample of the target group, and expressed as the median, in µg/L.

1.2.3 Pathology

If dietary iodine is severely deficient during pregnancy, both the mother and fetus will be at increased risk of hypothyroidism. If dietary iodine is moderately deficient during pregnancy, the mother may remain euthyroid, but the fetus is at increased risk of hypothyroidism (6). The maternal thyroid gland responds to iodine deficiency by hyperplasia and an increase in the trapping of iodine, as well as the preferential synthesis of T3 over T4. Thus, maternal TSH and T3 concentrations may fall slightly but remain within the normal reference range. But at the same time, because fetal brain T3 is generated from maternal T4, local hypothyroxinemia may occur in the developing brain of the fetus, and this is likely responsible for the neurodevelopmental damage seen in iodine deficiency (9). Later in pregnancy, due to decreased iodine supply to the fetal circulation, there is a decreased synthesis and secretion of T3 and T4 by the fetus and this can contribute to fetal hypothyroidism later in pregnancy. Since this is associated with a compensatory increase in concentrations of fetal TSH, neonatal TSH can be used as index for iodine deficiency in late pregnancy (Guthrie Test).

Infertility, abortions and stillbirth have been associated with iodine deficiency in areas with severe deficiency (10-12). The most severe consequence of *in utero* iodine deficiency for the offspring is cretinism. The neurological form of cretinism is more common than the myxedematous form. The putative pathogenesis of neurological cretinism is severe fetal hypothyroidism in the first trimester, and includes mental retardation, defects of hearing and speech, squint, impaired voluntary motor activity, disorders of stance with spastic gait and ataxia (13).

Inadequate thyroid hormone production during fetal development impairs myelination, cell migration, differentiation and maturation. However, the effect on cognitive function of the offspring in areas with mild to moderate iodine deficiency remains unclear. Most earlier studies have focused on thyroid dysfunction, independent of iodine status. Haddow et al. in the U.S. found that the IQ scores of 7 to 9 year old children of mothers with subclinical hypothyroidism during pregnancy (an increased TSH in the second trimester) were 4 points lower compared to children from mothers with normal thyroid function during pregnancy (14). Pop et al. reported impaired infant development for up to two years in children with hypothyroxinemia (free T4 below the 10^{th} percentile at 12 weeks of gestation) compared to controls in the Netherlands (15). In both studies, iodine status was not assessed, and both the U.S. and the Netherlands were iodine sufficient at the time of the studies. A single small study has suggested the prevalence of attention deficit and hyperactivity disorders is higher in the offspring of women living in iodine-deficient areas than those in iodine-replete regions (16), but this finding needs confirmation.

Mild iodine deficiency may lead to lower birth weight. Alvarez-Pedrerol et al. studied the association of birth weight and iodine status of 234 Spanish mothers in late pregnancy (17). Women with UIC between 100-149 µg/L in the third trimester had a lower risk of having a small-for-gestational-age newborn compared to mothers with urinary iodine concentrations below 50 µg/L (adjusted OR : 0.15 (95% CI: 0.03-0.76)). These results are in line with findings in school- and pre-school children from iodine-deficient areas where retarded growth has been observed (18, 19). Preterm newborns are particularly vulnerable to hypothyroidism because they no longer benefit from maternal thyroid hormones while their own thyroid glands are not yet fully functional (20). The breast milk or infant formula of preterm newborns should supply adequate iodine, and in some cases thyroid hormone replacement may be necessary.

1.2.4 Iodine supplementation

Controlled trials of iodine supplementation (100-200 µg/day) during pregnancy in mild-to-moderate iodine deficient areas have reported a significant increase in maternal UIC as well as smaller maternal and newborn thyroid glands with iodine, compared to the control group (13). However, none of the studies showed a clear effect of iodine supplementation on maternal and newborn total or free thyroid hormone concentrations. Thus, available data suggests that, in areas of mild-to-moderate iodine deficiency, the maternal thyroid is able to adapt to meet the increased thyroid hormone requirements of pregnancy (11), but controlled intervention trials measuring long-term clinical outcomes of mild iodine deficiency during pregnancy are now underway.

Moleti et al. studied the influence of long-term and short-term supplementation with iodized salt in an area of mild iodine deficiency (21). They compared the thyroid function of 62 women with regular iodized salt intake for at least two years with 38 women who commenced iodized salt consumption upon becoming pregnant. The incidence of maternal thyroid failure was six-fold higher in short-term users than in long-term users. These findings suggest that the prolonged use of iodized salt before pregnancy may increase thyroidal iodine stores and maintain normal maternal thyroid function during pregnancy.

1.2.5 Salt and preeclampsia

Preeclampsia is a pregnancy disease caused by a dysregulation of the vessels leading to increase of blood pressure, proteinuria as well as thrombocytemia. Clinical symptoms are headache and progressive oedema. The association with oedema led to the assumption that salt intake may play a role in the pathology of preeclampsia. Duley et al. reviewed in 2005 all available studies on the influence of salt intake on preeclampsia (22). They found two relevant trials, including 603 women, which both compared advice to reduce dietary salt intake with advice to continue a normal diet. The confidence intervals were wide and crossed the no-effect line for the risk for preeclampsia (relative risk 1.11, 95%CI 0.46 - 2.66). The authors concluded that salt consumption during pregnancy should remain a matter of personal preference. Thus, salt should not be restricted during pregnancy to reduce risk of preeclampsia, and this should not influence intake of iodine from iodized salt.

1.2.6 Iodine status in Swiss pregnant women

In Switzerland, iodine status in pregnancy is monitored every five years in national surveys (23). Details of these surveys are given in Chapter 3 of this report; in the last two surveys, in 2004 and 2009, the median UIC in pregnant women indicated iodine sufficiency. The most commonly used prenatal multivitamin supplements in Switzerland do not contain iodine (**Table 1**). And, as summarized in Chapter 3, only a small minority of pregnant women take prenatal supplements containing iodine. Therefore, the iodine fortification of Swiss salt supplies pregnant women with sufficient iodine and additional iodine supplementation is not recommended at this time for healthy women eating typical Swiss diets. However, iodine supplementation during pregnancy appears to be safe, even for those women already consuming iodized salt, and does not increase the incidence of post partum thyroid dysfunction (24). The effects of increasing iodine intakes in populations and iodine excess are covered in detail in Section 3.4 of Chapter 3 of this report. Iodine supplementation during pregnancy is recommended in several other countries where iodine intake is borderline sufficient or is deficient, including Germany, the U.S., New Zealand and Australia (25).

Table 1: Content of iodine in pregnancy supplements commonly-used in Switzerland.

Product	**Iodine content (recommended 250ug/day)**
Elevit pronatal©	0
Vitana©	0
Andreavit©	200ug
Gynefam Classic©	150ug
Femibion 400©	150ug
Burgerstein© (2 pills)	150ug

1.3. Lactation

1.3.1 Iodine requirements

WHO/ICCIDD/UNICEF recommend an intake of 250 µg/day of iodine for lactating women and propose a median UIC >100 µg/l in lactating women indicates iodine sufficiency (32). Iodine is secreted into the breast milk with a concentration gradient of 20 to 50 times that of plasma levels, through the increased expression of the sodium/iodine symporter (NIS) in lactating breast cells (26-28). Colostrum contains higher iodine concentrations (approximately 200-400 µg/l) than mature milk (29).

1.3.2 Iodine concentrations in breast milk

The iodine content of breast milk in iodine sufficient areas has been reported to be as high as 150-180 µg/l (33). However, there is no consensus on the optimal breast milk iodine concentration. An Austrian study by Tiran et al. showed that two years consumption of iodized table salt (10-20 ppm) doubled the median iodine concentration in breast milk (34). Iodine supplements may increase the iodine content of breast milk, although studies are contradictory (35, 36). The supplementation of breastfeeding mothers in iodine deficient areas with 150 µg per day of iodine during the first six

months of lactation did not increase breast milk iodine levels high enough to meet the requirements of the newborn (30). Iodine concentrations in breast milk may vary by infant's age and the stage of lactation. Substantial diurnal and day-to-day variations in breast milk iodine concentrations have been reported (31).

1.3.3 Iodine status during lactation in Switzerland

As discussed in detail in Chapter 3 of this report, the 2009 national Swiss iodine study included for the first time both lactating and non-lactating mothers of 6 to 12 month-old infants (23). Their overall median UIC was 75 µg, which may indicate borderline low intake, and was less than half of the median UIC in Swiss pregnant women. Only 5% of women reported the use of iodine supplements. Not all mothers were still breastfeeding at the time of the study and there was no significant difference in the median UIC comparing breastfeeding mothers vs. nonbreastfeeding mothers (67 ug/L, n=196 vs. 81 µg/L, n=311). The low iodine status of these women can likely be explained by the combined high iodine demands of both pregnancy and lactation. The median iodine concentration in breast milk in the 2009 survey was 49 µg/kg, somewhat lower than in a previous Swiss study reporting breast milk concentrations of 60 - 80 µg/L (22). Thyroid hormone levels were not investigated in the above study.

1.4. Infancy

1.4.1 Iodine requirements

The daily requirements of iodine have been estimated to be at least 15 µg/kg in full term neonates and 30 µg/kg in preterm infants. A daily intake of 90 µg of iodine is recommended by WHO to cover the newborn's needs (see **Table 3** in Chapter 2 of this report) (32). The iodine stores of a newborn are small and the thyroidal turnover rate of iodine is more rapid in infants than in adults (13). Therefore, during the breastfeeding period, the newborn is nearly completely dependent on iodine intake through breast milk and it is critical that mothers have adequate iodine levels. WHO/ICCIDD/UNICEF propose a median UIC >100 µg/l in infants indicates iodine sufficiency (32).

1.4.2 The importance of iodine in weaning foods

Bottle-fed infants usually have higher UIC levels than exclusively breast-fed infants due to the frequent supplementation of iodine in baby formulas (32). As discussed in Chapter 3 of this report, in Switzerland in 2009, breast-fed infants had a lower median urinary iodine concentration than non-breast-fed infants (82 µg/L vs. 105 µg/L; $p<0.001$) (23). Iodine content in formula is regulated in Switzerland by a directive, requiring 10 to 50 µg/100 kcal (33). Andersson et al. tested twelve of the most commonly used formula milks in Switzerland and found iodine contents ranging from 4.5 to 14.8 µg/100ml of milk (**Table 2**). A similar review of commercial foods in Germany reported milk (including breast milk, formula and milk from porridge) contributed significantly to iodine intake during the weaning period (34).

Weaning infants fed home-prepared complementary foods may be at risk of iodine deficiency, because pediatric experts recommend not to add salt to complementary foods and not to feed cow's milk to infants less than one year. These are the two most important sources of iodine in the diets of most industrialized countries, such as Switzerland, with iodized salt programs. This was supported by

the study of Swiss infants by Andersson et. al., where the median UIC in breast-fed weaning infants not receiving formula and/or complementary foods was significantly lower than infants receiving formula (70 vs. 109 µg/L) (23).

Table 2: Comparison of labeled and measured iodine concentrations in different brands of formula milk and infant cereals (23)

	Iodine concentration[1]			
Brand/ Product specification	Labeled [µg/100 kcal][2]	Labeled [µg/100 ml]	Measured [µg/100 ml][3]	Difference [%][4]
Infant formulas[4]				
Bimbosan[a]	7.1	4.8	4.6	-3.3
Bimbosan Bio[a]	7.7	5.2	4.5	-13.2
Follow-on formulas[5]				
Adapta 2[b]	14.5	10	9.1	-8.8
Coop Naturaplan Bio Galactina 2[c]	14.7	10	12.6	26.5
HiPP Folgemilch 2[d]	14.3	11	11.6	5.8
Holle Bio 2[e]	9.3	7	9.4	34.3
Milupa Aptamil 2[f]	17.6	12	13.2	10.0
Milupa Aptamil HA 2[†]	19.1	13	11.1	-14.6
Milupa Milumil 2[†]	19.1	13	11.5	-11.5
Nestlé Beba 2[g]	23.9	16	14.8	-7.6
Nestlé Beba HA 2[g]	14.9	10	9.3	-6.9
Soy-based formula				
Bimbosan Bisoja [a]	9.8	6.5	7.8	19.5
Instant milk-cereals *(to be prepared with water)*				
Milupa Miluvid plus[†]	19.1	36	33.5	-6.9
Nestlé Baby Cereals Vollkorn mit Früchten[g]	8.5	18	18.3	1.7
Nestlé Baby menu Milchgriess[g]	21.4	45	46.2	2.7
Instant cereals *(to be prepared with milk & water)*				
Galactina Ceralino Milchzusatz Getreide & Ovomaltine[c]	10.7	40[7]	37.4[8]	-6.5

1 Refers to product as prepared ready-to-eat
2 Calculated based on energy and iodine per 100 ml ready-to-eat product
3 Measured by inductively coupled plasma mass spectrometry (ICP-MS)
4 Percentage (%) of measured iodine concentrations compared to labeled iodine concentration based on µg/100 ml ready-to-drink product
5 Cow milk-based, HA = partially hydrolyzed milk proteins
6 Calculated based on energy and iodine per 100 g dry product, except for the Hipp ready-to-eat product

[7] Standard portion as indicated on the package, varying from 175 to 200 g
[8] µg/100g instant powder. Only water used for the preparation
[a-g] Products of
- [a] Bimbosan Ltd. (Welschenrohr, Switzerland)
- [b] Adapta (Lenzburg, Switzerland)
- [c] Coop (Basel, Switzerland)
- [d] HiPP GmbH (Sachseln, Switzerland)
- [e] Holle baby food GmbH (Riehen, Switzerland)
- [f] MILUPA SA (Domdidier, Switzerland)
- [g] Nestlé Suisse S.A. (Vevey, Switzerland)

1.5. Recommendations

- Because Swiss pregnant women overall are iodine sufficient, routine iodine supplementation during pregnancy is not needed for healthy women eating typical Swiss diets.
- For those Swiss pregnant women who may have low iodine intakes, a prenatal supplement containing 150-200 µg iodine per day may be indicated.
- Most prenatal supplements available in Switzerland do not contain iodine, and supplement manufacturers should be encouraged to include 150-200 µg iodine per day in their products.
- Swiss pregnant women who are consuming iodized salt can also safely consume a prenatal iodine supplement containing 150-200 µg iodine per day.
- Breastfed infants of iodine sufficient mothers obtain adequate iodine from breast milk and do not need supplemental sources of iodine. Once the infant has weaned from breast milk and is beginning to eat other foods, provision of iodine-fortified complementary foods, follow-on formula containing iodine and/or home-prepared foods containing iodized salt, may be important to meet their iodine requirements.
- With the current fortification level of 20 ppm iodine in salt in Switzerland, iodine intakes are borderline sufficient in pregnant women and infants, but may be mildly deficient in non-pregnant and lactating women. These data suggest it would be prudent to increase the iodine concentration in Swiss salt to 25 ppm.
- Regular surveys on iodine status in pregnant women and infants in Switzerland are necessary to ensure adequacy in the face of changes in salt and food consumption practices.

1.6. References

1. Glinoer D. The importance of iodine nutrition during pregnancy. Public Health Nutr. 2007;10(12A):1542-6.
2. Williams GR. Neurodevelopmental and neurophysiological actions of thyroid hormone. J Neuroendocrinol. 2008;20(6):784-94. Epub 2008/07/08.
3. Kennedy RL, Malabu UH, Jarrod G, Nigam P, Kannan K, Rane A. Thyroid function and pregnancy: before, during and beyond. J Obstet Gynaecol. 2010;30(8):774-83. Epub 2010/12/04.

4. Skeaff SA. Iodine deficiency in pregnancy: the effect on neurodevelopment in the child. Nutrients. 2011;3(2):265-73. Epub 2012/01/19.
5. de Escobar GM, Obregon MJ, del Rey FE. Maternal thyroid hormones early in pregnancy and fetal brain development. Best Pract Res Clin Endocrinol Metab. 2004;18(2):225-48.
6. de Escobar GM, Obregon MJ, del Rey FE. Iodine deficiency and brain development in the first half of pregnancy. Public Health Nutr. 2007;10(12A):1554-70. Epub 2008/03/11.
7. Perez-Lopez FR. Iodine and thyroid hormones during pregnancy and postpartum. Gynecol Endocrinol. 2007;23(7):414-28.
8. Glinoer D. Maternal and fetal impact of chronic iodine deficiency. Clin Obstet Gynecol. 1997;40(1):102-16. Epub 1997/03/01.
9. Morreale de Escobar G, Obregon MJ, Escobar del Rey F. Role of thyroid hormone during early brain development. Eur J Endocrinol. 2004;151 Suppl 3:U25-37.
10. Cobra C, Muhilal, Rusmil K, Rustama D, Djatnika, Suwardi SS, et al. Infant survival is improved by oral iodine supplementation. J Nutr. 1997;127(4):574-8. Epub 1997/04/01.
11. Dillon JC, Milliez J. Reproductive failure in women living in iodine deficient areas of West Africa. BJOG. 2000;107(5):631-6. Epub 2000/05/29.
12. Pharoah PO, Buttfield IH, Hetzel BS. Neurological damage to the fetus resulting from severe iodine deficiency during pregnancy. Lancet. 1971;1(7694):308-10. Epub 1971/02/13.
13. Zimmermann MB. Iodine deficiency in pregnancy and the effects of maternal iodine supplementation on the offspring: a review. Am J Clin Nutr. 2009;89(2):668S-72S. Epub 2008/12/18.
14. Haddow JE, Palomaki GE, Allan WC, Williams JR, Knight GJ, Gagnon J, et al. Maternal thyroid deficiency during pregnancy and subsequent neuropsychological development of the child. N Engl J Med. 1999;341(8):549-55.
15. Pop VJ, Kuijpens JL, van Baar AL, Verkerk G, van Son MM, de Vijlder JJ, et al. Low maternal free thyroxine concentrations during early pregnancy are associated with impaired psychomotor development in infancy. Clin Endocrinol (Oxf). 1999;50(2):149-55. Epub 1999/07/09.
16. Vermiglio F, Lo Presti VP, Moleti M, Sidoti M, Tortorella G, Scaffidi G, et al. Attention deficit and hyperactivity disorders in the offspring of mothers exposed to mild-moderate iodine deficiency: a possible novel iodine deficiency disorder in developed countries. J Clin Endocrinol Metab. 2004;89(12):6054-60. Epub 2004/12/08.
17. Alvarez-Pedrerol M, Guxens M, Mendez M, Canet Y, Martorell R, Espada M, et al. Iodine levels and thyroid hormones in healthy pregnant women and birth weight of their offspring. Eur J Endocrinol. 2009;160(3):423-9. Epub 2008/12/31.
18. Koutras DA, Christakis G, Trichopoulos D, Dakou-Voutetaki A, Kyriakopoulos V, Fontanares P, et al. Endemic goiter in Greece: nutritional status, growth, and skeletal development of goitrous and non goitrous populations. Am J Clin Nutr. 1973;26(12):1360-8. Epub 1973/12/01.

19. Mason JB, Deitchler M, Gilman A, Gillenwater K, Shuaib M, Hotchkiss D, et al. Iodine fortification is related to increased weight-for-age and birthweight in children in Asia. Food Nutr Bull. 2002;23(3):292-308. Epub 2002/10/05.

20. LaFranchi S. Thyroid function in the preterm infant. Thyroid. 1999;9(1):71-8. Epub 1999/02/26.

21. Moleti M, Lo Presti VP, Campolo MC, Mattina F, Galletti M, Mandolfino M, et al. Iodine prophylaxis using iodized salt and risk of maternal thyroid failure in conditions of mild iodine deficiency. J Clin Endocrinol Metab. 2008;93(7):2616-21. Epub 2008/04/17.

22. Duley L, Henderson-Smart D, Meher S. Altered dietary salt for preventing pre-eclampsia, and its complications. Cochrane Database Syst Rev. 2005(4):CD005548. Epub 2005/10/20.

23. Andersson M, Aeberli I, Wust N, Piacenza AM, Bucher T, Henschen I, et al. The Swiss iodized salt program provides adequate iodine for school children and pregnant women, but weaning infants not receiving iodine-containing complementary foods as well as their mothers are iodine deficient. J Clin Endocrinol Metab. 2010;95(12):5217-24. Epub 2010/09/03.

24. Nohr SB, Jorgensen A, Pedersen KM, Laurberg P. Postpartum thyroid dysfunction in pregnant thyroid peroxidase antibody-positive women living in an area with mild to moderate iodine deficiency: is iodine supplementation safe? J Clin Endocrinol Metab. 2000;85(9):3191-8. Epub 2000/09/22.

25. aid. Ernährung in der Schwangerschaft - Handlungsempfehlungen KOMPAKT. 2011 [29.3.2012]; Available from: http://www.bmelv.de/SharedDocs/Downloads/Broschueren/Handlungsempfehlungen-fuer-Schwangere.pdf?__blob=publicationFile.

26. De La Vieja A, Dohan O, Levy O, Carrasco N. Molecular analysis of the sodium/iodide symporter: impact on thyroid and extrathyroid pathophysiology. Physiol Rev. 2000;80(3):1083-105. Epub 2000/07/14.

27. Tazebay UH, Wapnir IL, Levy O, Dohan O, Zuckier LS, Zhao QH, et al. The mammary gland iodide transporter is expressed during lactation and in breast cancer. Nat Med. 2000;6(8):871-8. Epub 2000/08/10.

28. Spitzweg C, Joba W, Eisenmenger W, Heufelder AE. Analysis of human sodium iodide symporter gene expression in extrathyroidal tissues and cloning of its complementary deoxyribonucleic acids from salivary gland, mammary gland, and gastric mucosa. J Clin Endocrinol Metab. 1998;83(5):1746-51. Epub 1998/05/20.

29. Etling N, Padovani E, Fouque F, Tato L. First-month variations in total iodine content of human breast milks. Early Hum Dev. 1986;13(1):81-5. Epub 1986/02/01.

30. Mulrine HM, Skeaff SA, Ferguson EL, Gray AR, Valeix P. Breast-milk iodine concentration declines over the first 6 mo postpartum in iodine-deficient women. Am J Clin Nutr. 2010;92(4):849-56. Epub 2010/08/13.

31. Kirk AB, Dyke JV, Martin CF, Dasgupta PK. Temporal patterns in perchlorate, thiocyanate, and iodide excretion in human milk. Environ Health Perspect. 2007;115(2):182-6. Epub 2007/03/27.

32. Azizi F, Smyth P. Breastfeeding and maternal and infant iodine nutrition. Clin Endocrinol (Oxf). 2009;70(5):803-9. Epub 2009/01/31.

33. Verordnung des EDI vom 23. November 2005 über Speziallebensmittel [14.12.2012]. Available from: http://www.admin.ch/ch/d/sr/c817_022_104.html;

34. Alexy U, Drossard C, Kersting M, Remer T. Iodine intake in the youngest: impact of commercial complementary food. Eur J Clin Nutr. 2009;63(11):1368-70. Epub 2009/08/13.

2. The effects of iodine deficiency on cognition and learning in children

Prof. Dr.med. Michael B. Zimmermann

The author declares no conflicts of interest.

2.1. Summary

The major impact of hypothyroidism due to iodine deficiency is impaired neurodevelopment, particularly early in life. In the fetal brain, inadequate thyroid hormone impairs myelination, cell migration, differentiation and maturation. Offspring of severely iodine deficient mothers are at high risk for cognitive disability, with cretinism being the most severe manifestation. It is less certain if mild-to-moderate iodine deficiency during childhood impairs cognitive function and learning, but the two most recent randomized controlled trials (18,19) have shown benefits on children's performance on cognitive tests. The positive results of these studies need to be replicated in other groups of mild-to-moderately iodine deficient children before firm conclusions can be drawn.

2.2. Introduction

Iodine is an essential component of the hormones produced by the thyroid gland. Thyroid hormones, and therefore iodine, are essential for mammalian life. In 1907, David Marine, a U.S. physician, showed that endemic goiter (thyroid enlargement due to iodine deficiency) was caused by iodine deficiency (ID); five years later, goiter prophylaxis using iodized salt was introduced in Switzerland (1). Iodine (as iodide) is widely but unevenly distributed in the earth's environment. In many regions, leaching from glaciations, flooding, and erosion have depleted surface soils of iodide. Crops grown in these soils will be low in iodine, and humans and animals consuming food grown in these soils become iodine deficient.

Soils in the mountainous regions of Switzerland have very low iodine content due to extensive glaciation. As a consequence, these regions, up until the early 1900s, were afflicted by severe endemic goiter and cretinism. Introduction of iodized salt has eliminated these disorders in Switzerland. ID has multiple adverse effects on growth and development in animals and humans. These are collectively termed the iodine deficiency disorders, and are one of the most important and common human diseases (2,3). They result from inadequate thyroid hormone production due to lack of sufficient iodine.

Worldwide, about 1.8 billion individuals still have insufficient iodine intakes, including nearly 1/3 of all school-age children (4). Iodine deficiency is not confined to developing countries, many industrialized countries are iodine deficient, including the United Kingdom and Australia, and it is estimated that ca. 40% of school-aged children in Europe have low iodine intakes (4). Recommended iodine intakes in children, as well as older age groups, are shown in **Table 3**.

Table 3: Recommendations for iodine intake (µg/day) by age or population group

Age or population group[a]	U.S. Institute of Medicine (ref.25)	Age or population group[c]	World Health Organization (ref.5)
Infants 0–12 months [b]	110-130	Children 0-5 years	90
Children 1-8 years	90	Children 6-12 years	120
Children 9-13 years	120		
Adults ≥14 years	150	Adults >12 years	150
Pregnancy	220	Pregnancy	250
Lactation	290	Lactation	250

[a] Recommended Daily Allowance
[b] Adequate Intake
[c] Recommended Nutrient Intake.

According to the World Health Organization (WHO), classification of iodine status in a population of school-age children should be based on the median UI concentration (UIC) (5). The concentration of iodine in urine is a good biomarker of recent iodine intake, because ca. 90% of dietary iodine is absorbed, and nearly all dietary iodine is ultimately excreted in the urine (3). As shown in **Table 4**, a UIC of 100-199 µg/L indicates optimal iodine nutrition in school-age children. In this review, mild iodine deficiency in a population of school-age children is defined as a median UIC of 50-99 µg/L, moderate iodine deficiency as a median UIC of 20-49 µg/L, and severe iodine deficiency as a median UIC of ≤19 µg/L (5).

Table 4: Epidemiological criteria from the World Health Organization (ref.5) for assessing iodine nutrition in a population based on median and/or range of urinary iodine concentrations.

Median urinary iodine (µg/L)	Iodine intake	Iodine nutrition
School-aged children		
<20	Insufficient	Severe iodine deficiency
20-49	Insufficient	Moderate iodine deficiency
50-99	Insufficient	Mild iodine deficiency
100-199	Adequate	Optimal
200-299	More than adequate	Risk of iodine-induced hyperthyroidism in susceptible groups
>300	Excessive	Risk of adverse health consequences (iodine-induced hyperthyroidism, autoimmune thyroid disease)
Pregnant women		
< 150	Insufficient	
150 – 249	Adequate	
250 – 499	More than adequate	
≥ 500	Excessive[a]	

Median urinary iodine (µg/L)	Iodine intake	Iodine nutrition
Lactating women[b]		
< 100	Insufficient	
≥ 100	Adequate	
Children less than 2 years old		
< 100	Insufficient	
≥ 100	Adequate	

[a] The term "excessive" means in excess of the amount required to prevent and control iodine deficiency.

[b] In lactating women, the figures for median urinary iodine are lower than the iodine requirements because of the iodine excreted in breast milk.

2.3. Iodine deficiency, hypothyroidism and the developing brain

In areas where dietary iodine intake is adequate, the healthy thyroid gland traps 60-80 µg of iodine/day to balance losses and maintain thyroid hormone synthesis (3). Below this level of thyroid uptake, the iodine content of the gland is depleted, and many individuals develop goiter. Goiter, an enlargement of the thyroid gland visible as an abnormal swelling at the base of the neck, develops in iodine deficient individuals because the thyroid increases its size in an attempt to filter more iodine from the bloodstream. In chronic iodine deficiency, thyroid hormone synthesis is limited by lack of iodine. This leads to low concentrations of thyroid hormone in the blood, a condition termed hypothyroidism. This can damage the developing brain (2,3).

Thyroid hormone receptors are present throughout the central nervous system and thyroid hormone has a myriad of important effects in the developing brain that include accelerated myelination and improved cell migration, differentiation and maturation (6). Hypothyroidism due to *in utero* iodine deficiency irreversibly impairs neural development in the hippocampus; the hippocampus is particularly important in learning in that it integrates spatial and contextual information (7). The detrimental effects of hypothyroidism on the developing brain depend on its timing, magnitude and duration. Early in the life cycle the brain is most vulnerable, but hypothyroidism has adverse effects on cognition even in adulthood (8).

Hypothyroidism due to severe iodine deficiency *in utero* can result in cretinism (2,3). There are two classic forms of cretinism – neurological and myxedematous (see Chapter 1 of this report). In areas of severe iodine deficiency, iodine treatment prevents cretinism and, in noncretinous offspring, improves psychomotor and developmental scores (3). Cretinism is no longer common due to the rapid expansion of programs of salt iodization worldwide, although it may still occur in remote areas. Therefore, the remainder of this paper will focus on the potential adverse effects of more mild iodine deficiency.

The cognitive deficits associated with iodine deficiency may not be limited to remote, severely iodine deficient areas. Experts have argued that even mild-to-moderate iodine deficiency in pregnancy, still present in many countries around the world, may affect cognitive function of the offspring. However,

this remains uncertain (12) (see Chapter 1 of this report). No well-controlled prospective studies have evaluated the effects of iodine repletion in mild-to-moderately deficient pregnant women on child cognitive or motor development. Because of this, the potential adverse effects of mild-to-moderate iodine deficiency during pregnancy on later childhood cognition and learning remain unclear.

2.4. Cross sectional studies in childhood

There have been many cross-sectional studies comparing cognition and/or motor function in children from chronically iodine deficient and iodine sufficient areas, including children from Asian and European backgrounds (13). These cross-sectional studies, with few exceptions, report impaired intellectual function and motor skills in children from iodine deficient areas. However, observational studies are often confounded by other factors that affect child development. Also, these studies could not distinguish between the persistent effects of *in utero* iodine deficiency and the effects of current iodine status.

2.5. Randomized controlled trials

Several early randomized, controlled trials in school-aged children tried to measure the effect of iodized oil on cognition (14-17) but methodological problems limit their interpretation. In a well-designed, placebo controlled, double-blind 6 month intervention trial, moderately iodine deficient 10-12 y-old children (n=310) in Albania (18) were randomized to receive either 400 mg of iodine as oral iodized oil or placebo. Treatment with iodine markedly improved iodine and thyroid status: at 24 wk, median UIC in the treated group was 172 µg/L and mean circulating T4 increased ≈40%. Compared to placebo, iodine treatment significantly improved information processing, fine motor skills, and visual problem solving (18).

Another carefully conducted, randomized controlled trial in 10–13 y children (n=184) in New Zealand (19) gave a daily tablet containing 150 µg iodine as KI or placebo for 28 wk. Cognitive performance was assessed through 4 subtests from the Wechsler Intelligence Scale for Children after 28 wk. Thyroid hormone concentrations were in the normal range at baseline for all children. Despite this, iodine improved scores on 2 of the cognitive tests: picture concepts ($P = 0.023$) and matrix reasoning ($P = 0.040$). Overall cognitive score of the iodine group was 0.19 SDs higher than that of the placebo group ($P = 0.011$) (19).

In these two studies (18,19), increasing iodine intakes over several months improved cognition in older children who presumably grew up under conditions of iodine deficiency. This short-term beneficial effect may have been due to improvements in myelination of central nervous system mediated by an increased supply of thyroid hormone (20). Myelinization continues throughout childhood particularly in the frontal cortex, the brain area responsible for higher-order cognition and fluid intelligence. Alternatively, better thyroid function could improve cognition by effects on neurotransmitters and/or glucose metabolism (21).

2.6. Meta-analyses

Two meta-analyses have been done to look at the effects of iodine deficiency on the Intelligence Quotient (IQ). In the first, the authors looked at the effect of iodine deficiency on mental development in both adults and children (22). They pooled data from 21 observational and experimental studies done in areas of moderate-to-severe iodine deficiency. The IQs of non-ID groups were on average 13.5 IQ points higher than those of the iodine-deficient groups. In a second meta-analysis by Qian et al. (23) that pooled data from studies in Chinese children, there was an increase of ≈12 IQ points for children born more than 3.5 years after iodine prophylaxis was introduced. Based on the close agreement of the overall effect in these two large meta-analyses, it appears moderate-to-severe iodine deficiency reduces the IQ by 12-13 points (22,23).

2.7. Recommendations

- School-age children (6-12 y-olds) have a daily iodine requirement of 120 µg/day
- The main exposure biomarker used to assess iodine intakes in schoolchildren is the median urinary iodine concentration (UIC), and a median UIC of 100-199 µg/L indicates optimal iodine nutrition in a population of school-age children. Chapter 3 of this report includes a discussion of the iodine status in school-age children in Switzerland.
- The clear benefits of iodine repletion in school-age children demonstrated in the New Zealand study (19) are particularly relevant for the European/Swiss setting, in that these children were only mildly deficient and came from middle-class backgrounds and school environments similar to that of many European children.
- Until more data become available, the prudent course is to ensure all school-aged children have ample iodine intakes and avoid even mild degrees of iodine deficiency.
- Switzerland is fortunate in this regard, because the long-running Swiss iodized salt program, a model for most other countries, has provided adequate iodine to school children in Switzerland for decades (see Chapter 3 of this report). But it is critical not to become complacent.
- Children are vulnerable to even short-term lapses in salt iodization programs (3), and the dietary iodine supply in Switzerland is influenced by many hidden factors (see Chapter 4 of this report).
- Regular monitoring of iodine status in children, with appropriate adjustments to the iodine content in salt if needed, will ensure this ancient scourge remains eliminated in Switzerland.

2.8. References

1. Marine D, Kimball OP. The prevention of simple goiter in man. A survey of the incidence and types of thyroid enlargements in the schoolgirls of Akron (Ohio), from the 5th to the 12th grades, inclusive--the plan of prevention proposed. 1917. J Lab Clin Med 1990;115:128-36.
2. Hetzel BS. Iodine deficiency disorders (IDD) and their eradication. Lancet 1983;2:1126-9.

3. Zimmermann MB, Jooste PL, Pandav CS. Iodine-deficiency disorders. Lancet 2008;372:1251-62.
4. Andersson M, Karumbunathan V, Zimmermann MB. Global iodine status in 2011 and trends over the past decade. J Nutr 2012 (in press).
5. World Health Organization UNICEF, International Council for Control of Iodine Deficiency Disorders. Assessment of iodine deficiency disorders and monitoring their elimination: a guide for programme managers. 3rd edition ed. Geneva: World Health Organization; 2007.
6. Bernal J. Thyroid hormones and brain development. Vitam Horm 2005;71:95.
7. Gong J, Dong J, Wang Y, Xu H, Wei W, Zhong J, et al. Developmental Iodine Deficiency and Hypothyroidism Impair Neural Development, Up-Regulate Caveolin-1 and Down-Regulate Synaptophysin in Rat Hippocampus. J Neuroendocrinol 2010;22:129-39.
8. Jensovsky J, Ruzicka E, Spackova N, Hejdukova B. Changes of event related potential and cognitive processes in patients with subclinical hypothyroidism after thyroxine treatment. Endocr Regul 2002;36:115-22.
9. Haddow JE, Palomaki GE, Allan WC, Williams JR, Knight GJ, Gagnon J, et al. Maternal thyroid deficiency during pregnancy and subsequent neuropsychological development of the child. N Engl J Med 1999;341:549-55.
10. Pop VJ, Kuijpens JL, van Baar AL, Verkerk G, van Son MM, de Vijlder JJ, et al. Low maternal free thyroxine concentrations during early pregnancy are associated with impaired psychomotor development in infancy. Clin Endocrinol 1999;50:149-55.
11. Oken E, Braverman LE, Platek D, Mitchell ML, Lee SL, Pearce EN. Neonatal thyroxine, maternal thyroid function, and child cognition. J Clin Endocrinol Metab 2009;94:497-503.
12. Zimmermann MB. Iodine deficiency in pregnancy and the effects of maternal iodine supplementation on the offspring: a review. Am J Clin Nutr 2009;89:668S-72S.
13. Santiago-Fernandez P, Torres-Barahona R, Muela-Martinez JA, Rojo-Martinez G, Garcia-Fuentes E, Garriga MJ, et al. Intelligence quotient and iodine intake: A cross-sectional study in children. J Clin Endocr Metab 2004;89:3851-7.
14. Bautista A, Barker PA, Dunn JT, Sanchez M, Kaiser DL. The effects of oral iodized oil on intelligence, thyroid status, and somatic growth in school-age children from an area of endemic goiter. Am J Clin Nutr 1982;35:127-34.
15. Huda SN, Grantham-McGregor SM, Tomkins A. Cognitive and motor functions of iodine-deficient but euthyroid children in Bangladesh do not benefit from iodized poppy seed oil (Lipiodol). J Nutr 2001;131:72-7.
16. Isa ZM, Alias IZ, Kadir KA, Ali O. Effect of iodized oil supplementation on thyroid hormone levels and mental performance among Orang Asli schoolchildren and pregnant mothers in an endemic goitre area in Peninsular Malaysia. Asia Pac J Clin Nutr 2000;9:274-81.
17. Shrestha R. Effect of iodine and iron supplementation on physical, psychomotor and mental development in primary school children in Malawi [doctoral thesis]. Wageningen: Wageningen Agricultural University; 1994.

18. Zimmermann MB, Connolly K, Bozo M, Bridson J, Rohner F, Grimci L. Iodine supplementation improves cognition in iodine-deficient schoolchildren in Albania: a randomized, controlled, double-blind study. Am J Clin Nutr 2006;83:108-14.

19. Gordon RC, Rose MC, Skeaff SA, Gray AR, Morgan KM, Ruffman T. Iodine supplementation improves cognition in mildly iodine-deficient children. Am J Clin Nutr 2009;90:1264-71.

20. Dussault JH, Ruel J. Thyroid hormones and brain development. Annu Rev Physiol 1987;49:321-4.

21. Isaacs E, Oates J. Nutrition and cognition: assessing cognitive abilities in children and young people. Eur J Nutr 2008;47:4-24.

22. Bleichrodt N, Born MP. A metaanalysis of research on iodine and its relationship to cognitive development. In: Stanbury FA, editor. <<The>> damaged brain of iodine deficiency cognitive, behavioral, neuromotor, educative aspects. New York [etc.]: Cognizant Communication Corporation; 1994. p. VII, 335 S.

23. Qian M, Wang D, Watkins WE, Gebski V, Yan YQ, Li M, et al. The effects of iodine on intelligence in children: a meta-analysis of studies conducted in China. Asia Pac J Clin Nutr 2005;14:32-42.

24. Deutsche Gesellschaft für Ernährung, Österreichische Gesellschaft für Ernährung, Schweizerische Gesellschaft für Ernährungsforschung, Schweizerische Vereinigung für Ernährung (Hrsg.) (2000). DACH-Referenzwerte für die Nährstoffzufuhr. Umschau/ Braus, 1. Auflage, Frankfurt am Main.

25. Institute of Medicine (IOM), Academy of Sciences, USA. Dietary reference intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium and Zinc. National Academy Press, Washington DC, 2001.

3. History and current epidemiology of iodine nutrition in Switzerland

Prof. Dr. med. Hans Bürgi and Dr. Maria Andersson

The authors declare no conflicts of interest.

3.1. Summary

Historically, Switzerland has proceeded cautiously with iodine fortification of salt, raising the iodine content of salt in four steps over a period of 90 years, from 3.75 ppm to the current level of 20 ppm iodide. The goiter rate in school-age children is now below 5% and no new cretins have been born since 1930. In the last two national surveys, in 2004 and 2009, the median UIC in school-age children and pregnant women indicated sufficient iodine intake. However, iodine intakes fell in these groups between 2004 and 2009. Thus, although Switzerland can now be considered an iodine sufficient country, free of goiter and cretins, iodine intakes appear to be decreasing, and are currently at the lower end of the recommended range in pregnant women and children. In addition, infants, lactating women and women of reproductive age have borderline low iodine intakes. Thus, these monitoring data suggest a modest increase in the iodine content of Swiss salt is needed in order to ensure iodine sufficiency in all population groups.

3.2. Historic epidemiology of iodine status

3.2.1 First epidemiologic surveys

For centuries, visitors to Switzerland were struck by the numerous inhabitants afflicted with goiter, sometimes combined with short stature, deaf-mutism and mental retardation. From the early 19th century onward the search for an etiology and treatment of this condition produced an appreciable scientific body of literature, which Merke, a surgeon from Basel, summarized in a superb volume in 1971 (1). In 1990, we updated Merke's Swiss data (2) and this review marks 80 years of uninterrupted use of iodized salt in Switzerland.

The frequent depiction of goiter and cretinism in older artworks in Europe indicates that the population was frequently affected by iodine deficiency. Rates of goiter in older records provide an estimate of the extent of iodine deficiency. Results of military drafts proved a rich source of such data. Not satisfied by the poor yields of the draft for the French army in the Département du Simplon (today the Swiss Canton du Valais), Napoleon ordered a census of cretins in 1810. It reported the high number of 4'000 cretins among a population of 70'000 (1).

Heinrich Bircher (3) compiled in an exhaustive monograph the tables and maps of goiter prevalence at recruitment in the years 1875 to 1880 for every single town and village in Switzerland, together with the prevalence of deaf-mutism and cretinism in selected areas. He concluded that goiter prevalence varied enormously from one village to another, even within the same county. Since military service is compulsory in Switzerland, all men must pass through a military medical board at age 19. In the years 1886 to 1891, 8 to 11% were found unfit for service due to a large goiter, with smaller goiters not being a reason for exemption (4). Theodor Kocher, the famous Bernese surgeon and Nobel Prize winner,

surveyed in 1883/84 all 76'606 schoolchildren of the Canton of Berne (5) and found that, depending on the location, the prevalence of goiter varied between 20 and 100%.

In a remarkable study, Als analyzed historical paintings and photographs of members of the aristocratic citizen's community of Berne, dating from the 16th to the 19th century (6). In the 2'356 individuals whose neck was visible in a portrait, she found evidence for goiter in 44% of women and 24% of men; the prevalence remaining stable over the four centuries covered by the study (6). Thus, although early studies on the epidemiology of iodine deficiency were not up to modern standards, the presence of historical goiter and cretinism in endemic proportion in Switzerland were documented beyond any doubt.

3.2.2 1922-23: The turning point

Bayard, a general practitioner in the valley of Zermatt, was convinced of the iodine deficiency theory of the etiology of goiter and believed side-effects of iodine treatment were due to inappropriately high dosages. In a dose-response study he personally provided 5 large families including their baker and their cattle with salt containing 3, 6, 9, 12 or 15 ppm of iodide. Noting that their goiters shrunk, he then supplied two entire villages with salt containing the lowest dose, after having established goiter size and prevalence among the 1'200 inhabitants. Then, the dose was raised at 6-month intervals in one of the two villages to 7.5 and then to 15 ppm of iodide. Bayard found that the lowest dose, which presumably provided roughly an additional 40 µg iodine per day, was capable of shrinking some, but not all goiters. The next higher dose (15 mg/kg) was more effective and was well- tolerated without adverse reactions (7, 8).

Eggenberger, chief surgeon at the hospital in Herisau, agreed with Bayard's dose recommendations and decided it was time to act. In 1922, he started a campaign of evening lectures in every single community of his small Canton of Appenzell Ausserrhoden and then collected 3'480 signatures for a petition to the government of the canton. Within one week the government approved a trial of universal salt iodization (9-11)! Eggenberger went to work immediately. With the help of family members he personally added 10 mg KI per kg salt (7.5 ppm iodide) using a simple hand-and-shovel method for mixing.

Within one year, in 1923, existing goiters had shrunk in 66% of the schoolchildren whose families used iodized salt on a regular basis, compared with only 28% in those families who did not. Estimated mean thyroid gland weight in children entering primary school diminished from 21 to 13 g, and the presence of a palpable thyroid gland in newborns, originally affecting 50% of newborns, had entirely disappeared (11-13). In November 1922, the United Swiss Rhine Salt Works, the exclusive supplier to 24 of 25 cantons, took up production of salt containing 5 mg KI (3.75 ppm iodide) per kg.

3.2.3 The Swiss Goiter Commission and dose problems

In 1922, the Swiss Federal Office of Public Health installed the Swiss Goiter Commission, which included most persons engaged in goiter research in Switzerland. On June 24, 1922 the Commission recommended to the 25 Cantons to take up the sale of salt containing 2.5 to 5 mg KI (1.9-3.75 ppm iodide) per kg on a voluntary basis, with non-iodized salt remaining available (14, 15). Eggenberger correctly predicted that this dose would turn out to be too low to eradicate goiter completely, but it was

a compromise to which even the opponents of iodized salt could agree. The Swiss Goiter Commission convened about once a year, it organized two big international goiter conferences in 1927 and 1933 in Berne and it monitored progress of the USI program.

Some members of the Commission were adamantly opposed to universal salt iodization (USI) and blocked its introduction in some cantons, as well as the dose increase in some other cantons. Some cantons complied reluctantly, and not before 1955 all cantons had agreed. Side-effects of hyperthyroidism (iodine-induced hyperthyroidism) were closely monitored, but could not be observed in epidemiological studies. Even though urinary iodine excretion in the 1930s showed persisting moderate iodine deficiency (**Table 5**), the Commission was unable to agree on higher salt iodine content in Switzerland and the Swiss Goiter Commission thereupon stopped its activities. Finally, in 1962, the Swiss Rhine Salt Works, frustrated with having to produce salt with different specifications for every canton, decided on its own to increase the iodide content of salt from 3.75 to 7.5 ppm.

Table 5: Overview of field studies in Switzerland from 1923 to 2009.

Year	Iodine in salt (mg/kg)	Iodine in urine (µg/L)	Population and sample size	Reference
1923	None	18	23 inhabitants of 2 goitrous villages	(35, 36)
1939	3.75	36	Goitrous and non goitrous adults Canton Berne	(37)
1975	7.5	<100[1]	Patients hospitalized in 1975	(16)
1979	7.5	76-93	Healthy adults	(17)
1981-1988	15	127-160	112 outpatients and 245 school children	(2)
1984	15	97	112 healthy adults	(52)
1994	15	118[1]	214 school children Canton Solothurn	(38)
1997	15	96	243 school children from Zurich area and Engadine valley	(39)
1998	15	94	412 subjects in Bern region (infants, children, adolescents, adults and seniors)	(53)
1999	15-20	115	National sample of 600 school children	(19)
2004	20	141	National sample of 386 school children	(20)
2009	20	120	National sample of 916 school children	(21)

[1] µg/g creatinine

In the 1970s, available data suggested that this dose was still too low (16, 17). In 1980, the iodine content in salt was raised to 15 ppm iodide, without causing protests. In 1988, 92% of retail salt and 76% of all salt for human consumption (including food industry) was iodized, even though noniodized salt still remained available. Table 5 shows the effects of increasing the dose of iodine in salt on urinary iodine content. Since 1999, the median urinary iodine concentration (UIC) has remained above

the limit of 100 µg/L set by the WHO (18). And since 1999 the Swiss iodine status is reassessed by a nationally-representative survey performed at 5-year intervals according to the WHO standards.

In 1977 the Fluorine Commission of the Swiss Academy of the Medical Sciences (that had existed since 1950) was additionally charged to address iodine nutrition in Switzerland and the iodized salt program. Renamed the Fluorine-Iodine Commission, it currently supervises the salt iodization program, reports to the Federal Office of Health and recommends adjustments to the salt iodine content when necessary.

3.3. Current epidemiology of iodine status

3.3.1 School children

Three national studies conducted in 1999, 2004 and 2009 evaluated the iodine status in 6 to 13 year old school children (19-21). The iodine intake is now overall adequate with a median UIC of 120 µg/L in children (21). **Table 4** in Chapter 2 shows the median UIC criteria for defining iodine status in different age groups and populations. The three nationwide studies demonstrate a stable optimal iodine status over the last 10 years (**Figure 2**). Adequately iodized salt is consumed by 80% of children and the measured median iodine content in collected salt samples (iodized) is 19.8 mg/kg (range: 15.1-33.0) (**Table 6**). In the 1999 study the prevalence of goiter was determined by measuring thyroid volume by ultrasound (19, 22). The goiter prevalence was 3.9%, confirming that the goiter prevalence is now below the WHO threshold of 5% (18) and hence no longer a public health concern in Swiss children.

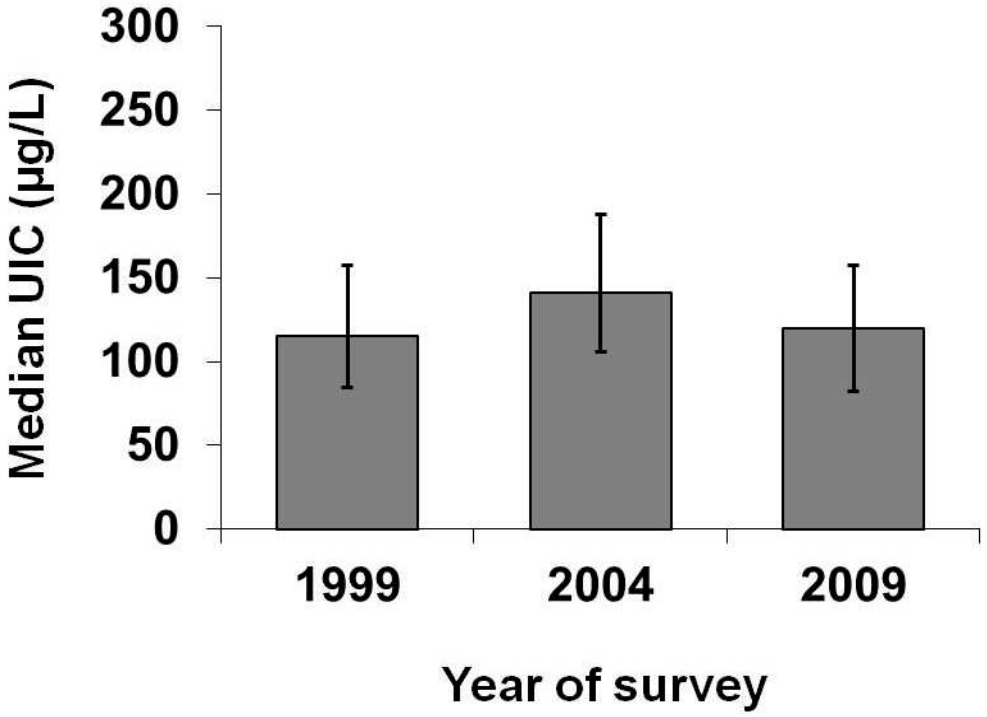

Figure 2: Median (25th, 75th percentiles) urinary iodine concentration in Swiss 6-12 y old children in 1999, 2004 and 2009[1,2].

[1] The shaded grey box show the range of median UIC that indicates sufficient iodine status defined by WHO (18).

[2] Adapted from (19-21).

Table 6: Iodized salt use in Swiss school children and pregnant women during the last ten years.

Year	n	Iodized salt (%)	Iodine concentration[1] (mg/kg)	Reference
School children[2]				
1999[3]	105	87	13.7 ± 1.9[4]	(19)
2004	85	85	18.3 ± 3.0[4, 5]	(20)
2009	266	80	19.8 (15.1-33.0)[6]	(21)
Pregnant women[7]				
2009	648	74		(21)

1 Iodine concentrations in salt samples with iodine concentrations greater than 10 ppm (1999 and 2004) and 15 ppm (2009)
2 Iodine concentrations measured in collected salt samples
3 Zürich metropolitan area
4 Mean ± SD
5 Significant increase compared to 1999 ($P < 0.01$)
6 Median (range)
7 Questionnaire asking about the use of iodized salt

3.3.2 Pregnant women

The dietary iodine requirements increase by more than 50% during pregnancy (see Chapter 1 of this report) (18, 23). The iodine status in pregnant women was evaluated in the three national studies conducted in 1999, 2004 and 2009 (**Figure 3**) (19-21). The median UIC in the most recent study was 162 µg/L (95% CI 144-177) and the iodine intake is now adequate also in pregnant women (21). The percentage of pregnant women who reported using iodized salt was 74% (**Table 6**). Seventy-nine percent of the women were taking nutritional supplements, but only 15% were taking supplements containing iodine (**Table 7**). The use of iodine containing supplements during pregnancy has remained stable over the last 10 years and does not explain the intermediate increase in median UIC in 2004 (**Figure 3**).

Table 7: Prenatal supplement use with and without iodine in Swiss pregnant women during the last ten years.

Year	Prenatal supplement use (%)	Prenatal supplement use with iodine (%)	Reference
1999	70	13	(19)
2004	62	9	(20)
2009	79	15	(21)

Thyroid volume and goiter prevalence have not been measured in pregnant women. However, unpublished thyroid function data from the 2009 study show no cases of hypo- or hyperthyroidism using the normal ranges of 0.2-4.0 mU/L for thyrotropin (TSH) and 100-200 nmol/L for thyroxin (T4) levels (24). The median TSH and T4 concentrations were 0.63 mU/L (range: 0.3-2.59) and 107 nmol/L (range: 21.2-199), respectively.

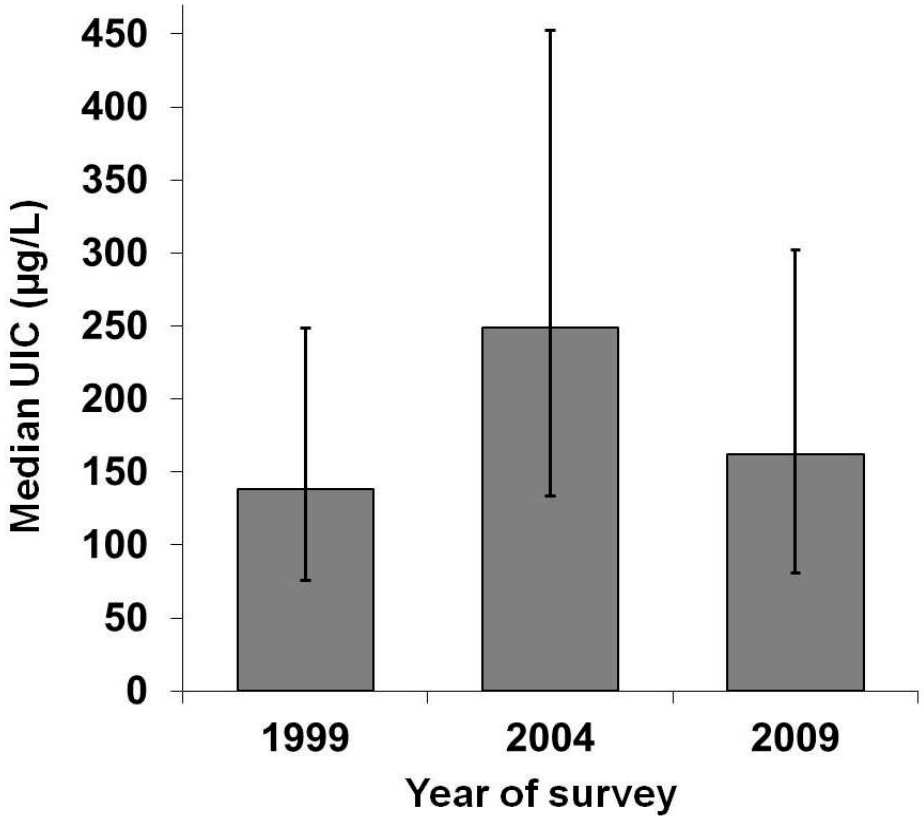

Figure 3: Median (25th, 75th percentiles) urinary iodine concentration in Swiss pregnant women in 1999, 2004 and 2009[1,2].

[1] The shaded grey box show the range of median UIC that indicates sufficient iodine status defined by WHO (18).

[2] Adapted from (19-21).

Thyroglobulin (Tg) is another sensitive marker of iodine status and thyroid function as elevated values reflect increased TSH stimulation due to iodine deficiency. WHO recommends Tg as a complementary marker to UIC to monitor iodine nutrition in children (18). Tg may be useful also in adults (25) and in pregnant women (26). The measurement of Tg in dried blood spots (DBS) has been developed for large population studies and is simple to use in the surveillance of iodine status in routine obstetric check-ups. We measured DBS-Tg in pregnant women in the 2009 study and the median Tg concentration was 8.0 ng/mL (range: 0.0-121). Reference ranges are available for school children (27), but not yet for adults or pregnant women. However, studies in iodine replete and iodine deficient populations of pregnant women suggest that Tg remains at pre-pregnancy concentration in iodine sufficiency, but increases in iodine deficiency (28-30). Using the reference ranges for children (3-40 ng/L), only 2.3% of all women had Tg levels above 40 ng/L. This agrees with the assumption that no more than 5% of subjects should have elevated Tg levels in an iodine sufficient population and confirms appropriate thyroid function in Swiss pregnant women.

3.3.3 Women of reproductive age

A recent study of female students (n=683) at the ETH Zürich reports a median UIC of 79 µg/L (range 3-621), indicating borderline low iodine intakes using present WHO criteria for UIC to assess iodine status in adults (**Figure 4**) (31). However, we have recently questioned the validity of the present

WHO threshold of 100 µg/L for median UIC in adults (31). This cut-off was developed for children, but is likely too high for adults and should probably rather be approximately 60-70 µg/L. We suggest iodine status and the prevalence of inadequate iodine intake should be evaluated in this age group based on the Estimated Average Requirement (EAR) cut-off point method. Using this approach, as described in reference 31, only 7% of the young women in the ETH study have inadequate iodine intakes.

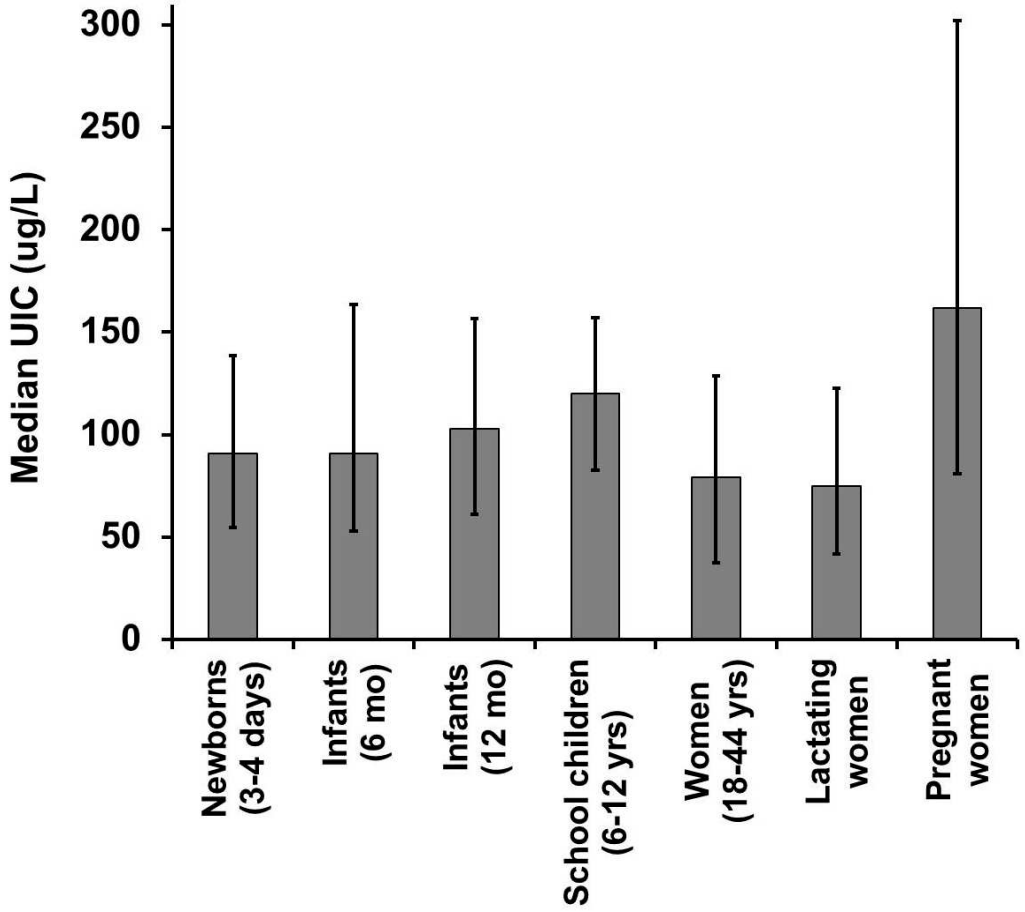

Figure 4: Present iodine status in the Swiss population1,2. Data presented as medians (25th, 75th percentiles).

[1] The shaded grey boxes show the ranges of median UIC that indicate sufficient iodine status defined by WHO (18).

[2] Adapted from (21, 31)

3.3.4 Lactating women

Lactating women have high iodine requirements as extra iodine is needed due to its excretion into the breast milk (23). The iodine status was measured for the first time in a national study of 507 mothers of weaning infants in 2009 (21). The median UIC of the mothers was 75 µg/L (95% CI 69-81) and the breast milk iodine concentrations (BMIC) in the women who were still breastfeeding was 49 µg/kg. Eighty four percent used iodized salt, but only 3% used iodine containing supplements. The median UIC of lactating women did not significantly differ from non-lactating mothers (67 µg/L, n=196 vs. 81 µg/L, n=311) and agrees well with the UIC reported in women of reproductive age. The WHO

threshold for defining iodine sufficiency in lactating women is 100 µg/L, the same as that for non-pregnant adult women (32). The iodine excreted in breast milk accounts for the difference between the higher dietary iodine requirements and the iodine excreted in the urine. Considering the discussion of UIC thresholds above, it is unclear if a median UIC of 75 µg/L indicates iodine deficiency during lactation.

3.3.5 Newborns and infants

The iodine status of newborns and weaning infants was evaluated in two studies, one by Dorey and Zimmermann in 2005 (33) and another by Andersson et al. in 2009 (21). UIC was measured in three separate national samples of infants during the first week of life, at 6 months and 12 months of age. The median UIC was 91 µg/L (95% CI 82-99) in newborns, 91 µg/L (95% CI 79-103) in 6 months olds and 103 µg/L (95% CI 92-116) in 12 months old children (**Figure 4**).

The study showed that breast-fed weaning infants may be at risk of inadequate iodine intakes due to the rather low BMIC. Median UICs in breast-fed weaning infants (82 µg/L) was lower than in non-breast-fed infants (105 µg/L) ($p < 0.001$). Iodine containing follow-on infant formula milks may be a complementary dietary iodine sources during the weaning period. About 60% of all infants were occasionally or regularly receiving one or more meals of infant formula milk and their median UIC was higher than those not receiving iodine containing infant formula milk (109 µg/L, n=304 vs. 73 µg/L, n=203) ($p<0.001$). However, the results do not suggest that iodine fortified infant formula milk is necessary to achieve optimal iodine nutrition in weaning infants. The median UIC in weaned infants fed homemade and/or complementary foods in glass jars was 89 µg/L in those not receiving breast milk or infant formula milk, but their UIC was not significantly different from to those who got breast milk and infant formula milk (109 µg/L, n=304). Breast milk is the most important iodine source during infancy and lactating women should be advised to consume iodized salt and choose foods produced with iodized salt. Breastfed infants of iodine sufficient mothers will obtain adequate iodine from breast milk and do not need supplemental sources of iodine.

The median UICs in newborns and 6 month old infants are just below the WHO UIC cut-off as shown in Figure 3; however, the study results are difficult to interpret. The iodine requirements in infants are poorly defined and the UIC to define sufficiency is uncertain. The current recommended dietary iodine intake for 0-6 month old infants (110 µg/day) is an adequate intake (AI) because there is insufficient data to establish an EAR for this age group. This AI is based on the iodine intake in breast fed infants from BMIC measured in U.S women during a period when overall iodine intakes in the U.S. population were excessive and the AI may be too high. The WHO recommends iodine intakes at this age to be 90 µg/day, slightly lower. We are currently planning a metabolic balance study in 2-3 month old infants to define the EAR and thresholds for UIC in this age group.

The newborn screening program routinely measures TSH in newborns on days 3 and 4 after birth. Zimmermann et al. (20) evaluated the neonatal screening program for Eastern Switzerland in 2005 and showed that the prevalence of newborn TSH <5 mU/L decreased from 2.9 % in 1992-1998 (before the increase in salt iodine concentration from 15 to 20 mg/kg) to 1.7% in 1999-2004 (after the increase) ($p < 0.0001$). These data confirm satisfactory thyroid function in young infants.

3.4. The effects of increasing iodine intakes in populations and iodine excess

European (40) and USA (41) expert committees have recommended tolerable upper intake levels for iodine (**Table 8**), but caution that individuals with chronic iodine deficiency may respond adversely to intakes lower than these. In monitoring populations consuming iodized salt, the World Health Organization/International Council for Control of Iodine Deficiency Disorders (WHO/ICCIDD) recommendations for the median UIC that indicates more-than adequate and excess iodine intake in school age children are 200-299 µg/L and >300 µg/L, and the median UIC that indicates excess iodine intake in pregnant women is >500 µg/L (18).

Table 8: Tolerable upper intake level for iodine (µg/day)

Age group	European Commission/Scientific Committee on Food (40)	US Institute of Medicine (41)
1–3 y	200	200
4–6 y (4-8 y)[1]	250	300
7–10 y (9-13 y)[1]	300	600
11–14 y	450	…
15–17 y (14-18y)[1]	500	900
Adult	600	1100
Pregnant women	600	1100

Age categories in parenthesis are for the tolerable upper level defined by US Institute of Medicine (41).

In areas of iodine sufficiency, such as Switzerland, most healthy adults are remarkably tolerant to iodine intakes up to 1 mg per day, as the thyroid is able to adjust to a wide range of intakes to regulate the synthesis and release of thyroid hormones (42). However, doses of iodine in the 200-500 microgram range may cause hyper- or hypothyroidism in those with past or present thyroid abnormalities. Signs and symptoms of iodine-induced hyperthyroidism include weight loss, rapid and irregular heartbeat, difficulty sleeping, fine tremor and anxiety. This occurs because, in a damaged thyroid gland, the normal down-regulation of iodine transport into the gland may not occur. Thus, even in so-called iodine sufficient populations, because some individuals will have past or present thyroid disorders, it is to be expected that changes in population iodine intake will affect the pattern of thyroid diseases.

Epidemiological studies on the relationship between iodine intake and the thyroid diseases have reported that populations with long-standing mild to moderate iodine deficiency demonstrate a high prevalence of thyroid hyperfunction but a low prevalence of thyroid hypofunction, while populations in areas of high iodine intake show the opposite pattern (43, 44). In mildly iodine deficient areas, there is an increase in thyroid multinodularity in females with advancing age that results in more cases of toxic nodular goiter (45, 46). Thus, like diffuse goiter, thyroid hyperfunction is part of the spectrum of disorders caused by mild-to-moderate iodine deficiency.

The overall incidence of differentiated thyroid carcinoma in populations does not appear to be influenced by iodine intake. Some studies have suggested the distribution of the subtypes of thyroid carcinoma is related to iodine intake; in areas of higher iodine intake, there appear to be fewer of the more aggressive follicular and anaplastic carcinomas, but more papillary carcinomas (47). When iodine prophylaxis is introduced in populations, this shift toward less malignant types of thyroid cancer, as well as a lower radioactive iodine dose to the thyroid in case of nuclear fallout, are benefits of the correction of mild-to-moderate iodine deficiency.

Increasing iodine intakes in iodine-deficient populations is typically accompanied by a rise in the incidence of hyperthyroidism. In Switzerland in 1980, when the population was mildly deficient and the iodine content of salt was raised from 7.5 to 15 ppm, the UIC increased from ≈ 80 to 150 µg per gr creatinine. In the first 2 years after this increase, the incidence of toxic nodular goiter rose by 12%, but gradually regressed to a stable level at only 25% of the initial incidence (48). The magnitude of the increase in iodine-induced hyperthyroidism (IIH) in populations depends on the amount of iodine administered and the severity of the pre-existing iodine deficiency. The increase in the incidence of IIH after a properly-monitored introduction of iodine is transient, because the resulting iodine-sufficiency in the population reduces the future risk of developing of autonomous thyroid nodules.

Denmark has documented the pattern of thyroid disease after careful introduction of iodized salt (49, 50). New cases of overt hypothyroidism were identified in two areas of Denmark with previous moderate and mild iodine deficiency, respectively (Aalborg, median UIC=45 µg/L; and Copenhagen, median UIC=61 µg/L) before and for the first 7 yr after introduction of a national program of salt iodization. The overall incidence rate of hypothyroidism modestly increased during the study period, from 38.3 to 47.2/100,000, with most cases in young and middle-aged adults. Similarly, new cases of overt hyperthyroidism in these two areas of Denmark before and for the first 6 yr after iodine fortification were identified. The overall incidence rate of hyperthyroidism increased from 102.8 to 138.7/100,000, with the increase occurring in both sexes and in all age groups. However, these data should be interpreted with some caution because the incidence rates for hypo- and hyperthyroidism in Denmark were already increasing before the introduction of iodized salt.

The current median UICs in school children and pregnant women in Switzerland are 120 µg/L and 162 µg/L, and the percentage of school-aged children above the UL of 300 µg/day was <1% in 2009. Thus, the current iodized salt program is not placing the Swiss population at risk for iodine excess. If the iodine content in Swiss salt were to increase ca. 20% (i.e. if the iodine level is increased from 20 to 25 ppm in 2013), there would still be very low risk of iodine excess. WHO/ICCIDD currently recommend to set salt iodization levels in national programs in the range of 20 to 40 ppm (18), and the Swiss fortification level is at the lower end of this recommended range.

More prospective data on the epidemiology of thyroid disorders caused by changes in iodine intake in other countries would be valuable. But it appears achieving optimal iodine intakes (in the range of 150-250 µg/d for adults) can minimize the amount of thyroid dysfunction in populations (51). Iodine prophylaxis with periodic monitoring is an extremely cost effective approach to help control thyroid disorders, compared to clinical diagnosis and treatment. If programs of iodine prophylaxis are carefully monitored for both iodine deficiency and excess, the relatively small risks of iodine excess are far

outweighed by the substantial risks of iodine deficiency — pregnancy loss, goiter, and mental retardation.

3.5. Conclusions

- In the last two national surveys, in 2004 and 2009, the median UIC in school-age children and pregnant women indicated sufficient iodine intake. However, iodine intakes fell in these groups between 2004 and 2009, and are currently at the lower end of the recommended range in pregnant women and children.
- Infants, lactating women and women of reproductive age have borderline low iodine intakes.
- The current iodized salt program is not placing the Swiss population at risk for iodine excess.
- The monitoring data suggest a modest increase in the iodine content of Swiss salt is needed in order to ensure iodine sufficiency in all population groups. Moreover, a modest increase in the iodine content of Swiss salt will not place the Swiss population at risk for iodine excess.

3.6. References

1. Merke F. Geschichte und Ikonographie des endemischen Kropfes und Kretinismus. Bern: H Huber, 1971.
2. Bürgi H, Supersaxo Z, Selz B. Iodine deficiency diseases in Switzerland one hundred years after Theodor Kocher's survey: a historical review with some new goitre prevalence data. . Acta Endocrinol (Copenh) 1990;123:577-90.
3. Bircher H. Der endemische Kropf und seine Beziehung zur Taubstummheit und Cretinismus. Basel: B Schwabe, 1883.
4. Hunziker H. Vom Kropf in der Schweiz. Corresp Blatt Schweiz Aerzte 1918;48:220-35 and 47-61.
5. Kocher T. Vorkommen und Vertheilung des Kropfes im Kanton Bern. Bern: KJ Wyss, 1889.
6. Als C, Stussi Y, Boschung U, Trohler U, Waber JH. Visible signs of illness from the 14th to the 20th century: systematic review of portraits. BMJ 2002;325(7378):1499.
7. Bayard O. Beiträge zur Schilddrüsenfrage. Basel: Benno und Schwabe, 1919.
8. Bayard O. Ueber das Kropfproblem. Schweiz Med Wochenschr 1923;53:703-7 and 32-7.
9. Eggenberger H. Das Vollsalz. Edtion ed. In: Hunziker H, ed. Die Prophylaxe der grossen Schilddrüse. Berne and Leipzig E. Bircher, 1924:284-322.
10. Eggenberger H. Die Verhütung des Kropfes und des Kropfrecidives. Schweiz Med Wochenschr 1923;53:245-9.
11. Eggenberger H. Kropf und Kretinismus. Edtion ed. In: Hirsch M, ed. Handbuch der Inneren Sekretion Vol 3. Leipzig: C. Kabitsch, 1928.
12. Zeller F. Resultate des ersten Jahres der freiwilligen Kropfbekämpfung in Appenzell a. Rh. Schweiz Med Wochenschr 1925;55:274-79.

13. Eggenberger H. 10 Jahre Kropfverhütung in Appenzell a. Rh. mit durchschnittlich 0.08 Milligramm Jod im täglichen Speisesalz. Bull Eidgen Gesundheitsamt 1933;18 (Suppl):9-16.

14. Schweizerische Kropfkommission (Swiss Goitre Commission). Proceedings of Meeting of June 24, 1922. Bull Eidgen Gesundheitsamt 1923;5 (Suppl):1-51.

15. Schweizerische Kropfkommission (Swiss Goitre Commission). Recommendations to the Cantonal Governments. Bull Eidgen Gesundheitsamt 1922;16:230-1.

16. Geiser J, Bürgi H, Grob PJ, Studer H. Bedeutung der Schilddrüsenkrankheiten in einer allgemein-internistischen Klinik. Schweiz Med Wochenschr 1978;108:1152-56.

17. Schmid M, Schulthess C, Burgi H, Studer H. Jodmangel ist in der Schweiz noch immer endemisch [Iodine deficiency is still endemic in Switzerland]. Schweiz Med Wochenschr 1980;110:1290-5.

18. World Health Organization, United Nations Children's Fund, International Council for the Control of Iodine Deficiency Disorders. Assessment of iodine deficiency disorders and monitoring their elimination. A guide for programme managers, 3rd edition. Geneva: World Health Organization, 2007.

19. Hess SY, Zimmermann MB, Torresani T, Burgi H, Hurrell RF. Monitoring the adequacy of salt iodization in Switzerland: a national study of school children and pregnant women. Eur J Clin Nutr 2001;55(3):162-6.

20. Zimmermann MB, Aeberli I, Torresani T, Burgi H. Increasing the iodine concentration in the Swiss iodized salt program markedly improved iodine status in pregnant women and children: a 5-y prospective national study. Am J Clin Nutr 2005;82(2):388-92.

21. Andersson M, Aeberli I, Wust N, et al. The Swiss iodized salt program provides adequate iodine for school children and pregnant women, but weaning infants not receiving iodine-containing complementary foods as well as their mothers are iodine deficient. J Clin Endocrinol Metab 2010;95(12):5217-24.

22. Hess SY, Zimmermann MB. Thyroid volumes in a national sample of iodine-sufficient swiss school children: comparison with the World Health Organization/International Council for the control of iodine deficiency disorders normative thyroid volume criteria. Eur J Endocrinol 2000;142(6):599-603.

23. Institute of Medicine, Academy of Sciences, USA. Dietary reference intakes for vitamin A, vitamin K, arsenic, boron, chromium, copper, iodine, iron, manganese, molybdenum, nickel, silicon, vanadium and zinc. Washington DC: National Academy Press, 2001.

24. Eckert M. Dried blood spot thyroglobulin to assess iodine status in school children and pregnant women. MSc thesis, ETH Zürich. Zürich: Swiss Federal Institute of Technology, 2010.

25. Vejbjerg P, Knudsen N, Perrild H, et al. Thyroglobulin as a marker of iodine nutrition status in the general population. Eur J Endocrinol 2009;161(3):475-81.

26. Laurberg P, Andersen S, Bjarnadottir RI, et al. Evaluating iodine deficiency in pregnant women and young infants-complex physiology with a risk of misinterpretation. Public Health Nutr

2007;10(12A):1547-52.

27. Zimmermann MB, de Benoist B, Corigliano S, et al. Assessment of iodine status using dried blood spot thyroglobulin: development of reference material and establishment of an international reference range in iodine-sufficient children. J Clin Endocrinol Metab 2006;91(12):4881-7.

28. Soldin OP, Tractenberg RE, Hollowell JG, Jonklaas J, Janicic N, Soldin SJ. Trimester-specific changes in maternal thyroid hormone, thyrotropin, and thyroglobulin concentrations during gestation: trends and associations across trimesters in iodine sufficiency. Thyroid 2004;14(12):1084-90.

29. Moleti M, Lo Presti VP, Campolo MC, et al. Iodine prophylaxis using iodized salt and risk of maternal thyroid failure in conditions of mild iodine deficiency. J Clin Endocrinol Metab 2008;93(7):2616-21.

30. Raverot V, Bournaud C, Sassolas G, et al. Pregnant French women living in the lyon area are iodine deficient and have elevated serum thyroglobulin concentrations. Thyroid 2012;22(5):522-8.

31. Zimmermann MB, Andersson M. Assessment of iodine nutrition in populations: past, present, and future. Nutr Rev 2012;70(10):553-70.

32. WHO Secretariat on behalf of the participants to the Consultation, Andersson M, de Benoist B, Delange F, Zupan J. Prevention and control of iodine deficiency in pregnant and lactating women and in children less than 2-years-old: conclusions and recommendations of the Technical Consultation. Public Health Nutr 2007;10(12A):1606-11.

33. Dorey CM, Zimmermann MB. Reference values for spot urinary iodine concentrations in iodine-sufficient newborns using a new pad collection method. Thyroid 2008;18(3):347-52.

34. König MP. Die kongenitale Hypothyreose und der endemische Kretinismus. Berlin, Heidelberg, New York: Springer-Verlag, 1968.

35. Von Fellenberg T. Das Vorkommen, der Kreislauf und der Stoffwechsel des Jods. Ergebn Physiologie 1926;25:295.

36. Von Fellenberg T. Ueber den Kreislauf des Jodes. Schweiz Med Wochenschr 1925;55:53-6.

37. Saegesser M. Schilddrüse, Jod und Kropf. Helv Med Acta 1939;6:Suppl 4.

38. Hoang Truong T, Gerber H, Haenel AF, Burgi H. Iodine supply at various periods in life and ultrasonographic thyroid volume in school children in a region of Switzerland (in German) [Jodversorgung in verschiedenen Lebensphasen und sonografische Schilddrüsenvolumina bei Schulkindern in einer Gegend der Schweiz]. Schweiz Med Wochenschr 1997;127(17):715-21.

39. Zimmermann MB, Hess S, Zeder C, Hurrell RF. Urinary iodine concentrations in swiss schoolchildren from the Zurich area and the Engadine valley. Schweiz Med Wochenschr 1998;128(20):770-4.

40. Scientific Committee on Food, Health and Consumer Protection Directorate-General. Opinion of the Scientific Committee on Food on the Tolerable Upper Intake Level of Iodine. SCF/CS/NUT/UPPLEV/26 Final. Brussels: European Commission, 2002.

41. Institute of Medicine, Academy of Sciences. Dietary reference intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium and Zinc. Washington DC: National Academy Press, 2001.

42. Chow CC, Phillips DI, Lazarus JH, Parkes AB. Effect of low dose iodide supplementation on thyroid function in potentially susceptible subjects: are dietary iodide levels in Britain acceptable? Clin Endocrinol (Oxf) 1991;34:413-6.

43. Laurberg P, Cerqueira C, Ovesen L, Rasmussen LB, Perrild H, Andersen S, Pedersen IB, Carlé A. Iodine intake as a determinant of thyroid disorders in populations. Best Pract Res Clin Endocrinol Metab. 2010;24(1):13-27.

44. Knudsen N, Bulow I, Jorgensen T, Laurberg P, Ovesen L, Perrild H. Comparative study of thyroid function and types of thyroid dysfunction in two areas in Denmark with slightly different iodine status. Eur J Endocrinol 2000;143:485-91

45. Knudsen N, Bulow I, Jorgensen T, Laurberg P, Ovesen L, Perrild H. Goitre prevalence and thyroid abnormalities at ultrasonography: a comparative epidemiological study in two regions with slightly different iodine status. Clin Endocrinol (Oxf) 2000;53:479-85.

46. Carlé A, Pedersen IB, Knudsen N, Perrild H, Ovesen L, Rasmussen LB, Laurberg P. Epidemiology of subtypes of hyperthyroidism in Denmark: a population-based study. Eur J Endocrinol. 2011;164(5):801-9.

47. Feldt-Rasmussen U. Iodine and cancer. Thyroid 2001;11(5):483-6

48. Burgi H, Kohler M, Morselli B. Thyrotoxicosis incidence in Switzerland and benefit of improved iodine supply. Lancet 1998;352:1034

49. Pedersen IB, Laurberg P, Knudsen N, Jørgensen T, Perrild H, Ovesen L, Rasmussen LB. An increased incidence of overt hypothyroidism after iodine fortification of salt in Denmark: a prospective population study. J Clin Endocrinol Metab 2007;92:3122-7

50. Bulow Pedersen I, Laurberg P, Knudsen N, Jørgensen T, Perrild H, Ovesen L, Rasmussen LB. Increase in incidence of hyperthyroidism predominantly occurs in young people after iodine fortification of salt in Denmark. J Clin Endocrinol Metab 2006;91:3830-4.

51. Zimmermann MB. Iodine requirements and the risks and benefits of correcting iodine deficiency in populations. J Trace Elem Med Biol 2008;22:81-92

52. Mordasini C, Abetel G, Lauterburg H, Ludi P, Perrenoud JP, Schmid H, Studer H. Sodium chloride intake and supply of iodine in the Swiss population [Article in German]. Schweiz Med Wochenschr. 1984;114(51):1924-9.

53. Als C, Keller A, Minder C, Haldimann M, Gerber H. Age- and gender-dependent urinary iodine concentrations in an area-covering population sample from the Bernese region in Switzerland. Eur J Endocrinol. 2000;143(5):629-37.

4. Sources of Iodine in Swiss Diets

Max Haldimann and Dr. Elizabeth Stalder

The authors declare no conflict of interest.

4.1. Summary

In Switzerland, the Federal Office of Public Health (BAG) measures the content of iodine in food groups to identify and quantify major sources of dietary iodine in the population. Nearly all foods, with the exception of marine fish, contain very low amounts of native iodine. Iodized salt, used as an ingredient in food production, is the main source of iodine in the Swiss diet. Good sources of dietary iodine are marine fish, bread, eggs, and dairy products. The mean iodine concentration in other foodstuffs, such as meat, vegetables and fruits, is extremely low. Overall, bread and dairy products are the main contributors of iodine intake. The high iodine content of milk is adventitious, originates largely from cattle feed and has been shown to vary strongly depending on season and use of iodine containing supplements. Cheese is an important nutritional source of iodine, yet most cheese producers have discontinued the use of iodized salt due to changes in labeling requirements for iodized salt and the inability to export products containing iodized salt. Iodized salt consumed from home-cooked food is only a small proportion of the total iodine intake since most of the salt consumption arises from consumption of processed foods. Therefore, consideration of any changes to the iodine salt content should be made with regard to the food industry rather than private households. A Swiss adult following the dietary recommendations of the Swiss Society for Nutrition and the Federal Office of Public Health will have an estimated mean iodine intake of ca.145 µg/day, close to the adult mean requirement of 150 µg/day recommended by the World Health Organization. However, people following a strict vegan diet without milk or eggs may be at risk of iodine deficiency, particularly if they do not use iodized salt. Nutritional habits, food formulation and production procedures are constantly changing, and since all of these factors can influence iodine intakes, regular monitoring of iodine nutrition in Switzerland remains important.

4.2. Introduction

Despite the serious effects of iodine deficiency in populations, few people are aware of the importance of maintaining sufficient iodine levels in their diet. Iodine in food and drinking water are virtually the only natural source of iodine for humans. In spite of this, direct measurements of food iodine content are rare in most countries. This is in part due to the fact that iodine intake can be indirectly assessed by an exposure biomarker, the measurement of urinary iodine excretion (1, 2). Another reason is that the determination of iodine in foods is an analytic challenge, especially at the relatively low concentrations that occur naturally.

However, detailed knowledge of the iodine content of foods nutrition is valuable in guiding nutrition policies to ensure adequate, but not excessive, iodine intakes in populations. In many industrialized countries, including Europe, iodine levels in the general population may be decreasing. Of the 40 European countries surveyed in a 2007 report, 19 have adequate iodine nutrition, 12 mild

deficiency, one moderate deficiency and there is insufficient data for eight countries (3). Ten years ago, the Federal Office of Public Health (BAG) initiated a study on iodine in food groups to identify and quantify major sources of dietary iodine (4). Chemical analysis of iodine was carried out on foods selected according to consumption frequency data of vital foodstuffs, including studies on cheese and milk (5, 6). This report is based on previous Swiss studies and new or unpublished data on foods. Special emphasis is thereby given to milk, cheese and bread.

4.3. Analysis of iodine in food

The peculiar chemistry of iodine turns the determination of iodine in foods into one of the most demanding tasks in modern nutrient analysis. Most of the popular procedures for iodine determination are based on the Sandell-Kolthoff reaction, which makes use of the catalytic effect of iodine in the oxidation-reduction process between cerium (IV) and arsenic (III). However, for samples other than urine this method is difficult to operate. Significant advances in the analysis of foods can be attributed to the advent of inductively coupled plasma mass spectrometry (ICP-MS). Unfortunately, the volatility of iodine and matrix effects of food samples hampers its quantification. To solve these problems, we developed a method based on isotope dilution analysis (7). In essence, the amount of iodine is calculated from the change of the isotope ratio induced by the addition of the long-lived radio isotope iodine-129, which is chemically the same substance. Thus, the susceptibility to errors is the same for both isotopes and the ratio remains unchanged. Unless stated otherwise, the iodine data given in this report were measured by isotope dilution ICP-MS at the BAG.

4.4. Iodine in the Environment

Iodine is one of the most abundant micronutrients in seawater, with concentrations of 50 to 60 µg/l. Iodine accumulates in seaweeds and algae, fish and shellfish (8). On land, the iodine content of water depends on the geochemical environment and leaching from the rock or soil into water sources. Subsequently, it is taken up by plants (to differing extents) and enters the food chain (9). Inland, mountainous regions, such as regions of Switzerland, are known to be typically iodine poor. Bee honey is regarded as an environmental indicator of trace element occurrence. Analysis of Swiss honey samples (10) showed low iodine contents, an indication that the soil is iodine poor (**Table 9**). In Switzerland, drinking water is a negligible source of iodine (11-13).

Table 9: Iodine concentration in basic food groups from the Swiss market.

Food Group	Iodine in dry food (µg/kg)					fresh food (µg/kg)	
	n	Mean	± SD	Median	P95 %[1]	Mean	Median
Cereals and grains							
Bread 1999 -2001	76	400	211	396	823	309	313
Bread 2011/12	64	482	73	479	589	347	346
Rice	5	34.7	20.8	36.9			

Food Group	Iodine in dry food (µg/kg)					fresh food (µg/kg)	
	n	Mean	± SD	Median	P95 %[1]	Mean	Median
Rice, processed	7	600	245	644			
Baked confectionery	13	245	260	148	741	206	126
Pasta	9	39.3	45.9	10.8			
Pasta containing whole egg	6	155	100	163			
Breakfast cereals	10	42.4	51	22			
Grain flour	10	35.7	11.2	36.6	47.0		
Potatoes	3	16	11	18		2.9	2.7
Meat and proteins							
Fish, marine	30	2591	2490	1594	6550	649	416
Fish, freshwater	17	375	436	205	1225	211	81.7
Egg, whole egg	6	1607	330	1526		325	303
Egg, industrial egg white powder	10	205	76.4	188	339		
Poultry	33	64.0	107	37.2	139	26.9	9.5
Beef	42	61.4	91.9	28.8	189	26.9	8.6
Veal	10	76.9	31.2	77.1	125	20.4	19.1
Pork	11	35.8	7.3	36.0	46.1	10.7	9.7
Game	7	33.8	1.5	32.7		9.1	8.5
Horse	11	63.4	54.5	46.4	166	17.5	12.0
Lamb	12	51.0	56.4	28.6	156	14.5	8.3
Vegetarian alternatives to meat	17	109	120	70	345	44.7	31.0
Sausages and processed meat	34	325	379	109	1093	179	48.4
Dairy products							
Milk 1997, year-round value [2]	20	855	323	792	1473	103	95.0
Milk 2007, September, farm level	197	587	467	459	1497	70.4	55.1
Milk 2011/12, Winter	28	915	257	967	1267	112	116
Milk 2012, September	18	585	199	579	849	70.2	23.9
Yoghurt	7	736	369	644		184	169
Quark	6	803	582	513		183	169
Cheese 2000, hard and semi-hard	17	545	298	454	1058	326	301
Cheese 2000, fresh and soft	8	303	208	191		117	101
Cheese 2011/12, hard, semi-hard [3]	49	192	143	150	442	119	93.0
Cheese 2011, fresh and soft	7					89.6	83.0
Vegetables and fruits							
Root and tuberous vegetables	16	65.8	54.6	34.5	162	7.3	4.1
Salads and leafy vegetables	23	228	184	152	557	11.0	7.1
Fruit vegetables	18	128	202	43.8	549	9.3	2.4

Food Group	Iodine in dry food (µg/kg)					fresh food (µg/kg)	
	n	Mean	± SD	Median	P95 %[1]	Mean	Median
Bulb and stem vegetables	8	50.6	30.5	34.9		4.8	3.2
Legumes	5	64.6	37.8	62.9		12.6	7.3
Canned and frozen vegetables	14	1351	1630	571	4787	109	110
Nuts	9	236	119	252			
Fresh fruit	62	18.2	14.5	14.7	44.2	2.7	2.0
Beverages							
Sweet soft drinks	13					16.1	8.0
Mineral water 2000	16					12.3	5.0
Mineral and drinking water 2012 [4]	9					1.5	1.1
Green Tea, leaves	6	119	90.2	90.2			
Miscellaneous							
Ready meals, canned or frozen	13	518	279	580	975	137	103
Ready meals, in PET trays [5]	5	214	133	201		59.7	67.9
Ready meal, fish in aluminum tray	1	3850		3850		1170	1170
Pizza, fresh	7	324	92.5	280		159	144
Dietary supplements	5	867	168	867			
Swiss honey	11	45.3	21.6	37.2	85.1	37.8	31.0
Mushrooms, dry	6	249	106	242			
Mushrooms, fresh	6	120	96.3	108		12.8	11.0

[1] 95 % percentiles are calculated when n ≥10
[2] large-batch samples from regional dairy factories
[3] average dry weight, calculated on the basis of the year 2000 samples (38 %)
[4] not carbonated
[5] PET (polyethylene terephthalate) package foods to be reheated in a microwave oven

4.5. Iodine in Food

The most recent data on iodine concentrations in Swiss foods are compiled in a study by Haldimann et al., which includes analysis of major food groups (4). These data have been regrouped in **Table 9** and are listed along with new and previously unpublished results. It is immediately clear that the richest sources of iodine in food are marine fish, bread, eggs, and dairy products. The mean iodine concentrations in other foodstuffs such as meat, vegetables and fruits are extremely low. Unlike humans or animals, plants do not require iodine. Therefore, the accumulation of iodine from soils is relatively poor as it merely reflects uptake from diffusion. Salads and leafy vegetables have somewhat higher iodine levels than other vegetables; however, the amounts of iodine are so minute that they are nutritionally insignificant. The same is true for fresh fruits. Fruits contain hardly any iodine at all, regardless of whether the origin is domestic or overseas.

The major natural food source of iodine is fish. Marine fish have much higher iodine content than freshwater fish because plankton accumulates iodine from the sea and serves as a food source for marine life. Consequently, native Swiss fish do not contain high levels of iodine. The iodine content of the flesh of fish is therefore in contrast to that of animals. It can be seen from comparison that eggs have a much higher content than poultry – indeed studies have shown that iodine supplementation of chicken feed enriches iodine content of eggs, but not of the meat (14). Similarly, the content of red meat is much lower than the content of dairy products. Interestingly, game has a similar level to both red meat and poultry, indicating that iodine ingested from "artificial" feed is not accumulated in muscle tissue. In pigs, only moderate dose-dependent iodine increases in edible tissues to varying feed supplementations have been observed (15).

4.5.1 Bread

Bread is a substantial dietary source of iodine in the Swiss diet. However, like most other plant products, grain does not derive much iodine from the soil. Thus, the high iodine content of bread is attributed to iodized salt, which is added to the dough prior to baking, as confirmed by our analysis. A wide variety of breads, including many regional specialties, are typical in Switzerland. The level of iodine concentration, however, does not depend on the type of bread. Since bread is a potential food vehicle for iodine fortification, we made an assessment of iodine stability during processing. We analyzed two samples of bread. Regular bread doughs, along with all the original ingredients and the resulting bread samples were obtained from bakeries. When the low iodine content of flour is considered, it is clear that the iodine contained in bread has iodized salt as its source. For one type of bread, a loss of 25 % was determined, for the second, 18 %. This is comparable to the figure cited by the WHO of an expected 20 % loss (16). Fielderova observed an even higher retention of >96 % iodide in bakery products (17). Iodine measurements of recent bread samples (**Table 9**) indicate that the level has not decreased over the last ten years ($p_{t;\,0.05} = 0.06$). Thus, the Swiss bread production practice that amounts to an average content of 1.85 % iodized salt has not changed (18). The bread market in Switzerland can be divided into that which is produced either industrially or in commercial bakeries; imported bread is negligible.

4.5.2 Milk

The iodine content of cow milk constitutes a considerable part of the iodine intake in humans. However, the high iodine content of milk originates largely from cattle feed and has been shown to vary strongly (5). Most of the cow fodder is plant matter, which varies greatly in composition and water content. As a rule, feeds of plant origin are poor in iodine and so it is added to meet the requirements of the dairy cows. Supplementary iodine in feed increases milk iodine concentration and this relationship has been established in dose-response studies (19). It is, however, possible that increases in milk iodine may be due to factors other than feed intake levels. Increased milk iodine due to teat dips have been reported (20). In Switzerland, iodophors as disinfecting agents are used mostly in post-milking dips (21) and so do not add appreciable amounts of iodine to the bulk milk (22).

The natural or background iodine concentration of milk varies with the time of year, concentrations of iodine being typically higher in winter months. Previous studies in Switzerland have consistently

demonstrated a considerable seasonal influence on the iodine content of raw milk. Schällibaum (23) presented several sets of monthly milk iodine values collected over the year. The lowest values occurred from May to October, whereas peak concentrations were found in February and March. In summer, when the dairy cows graze on pastureland, milk iodine concentration is significantly lower than in winter, when they are kept in the barn and given feeds fortified with iodine. Dairy cowherds that are kept indoors all year round tend to produce milk with higher iodine content (24). In addition, dairy cows produce less milk in the winter, causing a concentrating effect on iodine in the milk.

Apart from the seasonal effect, the relative amounts of iodine entering milk can vary considerably from farm to farm. Differences are attributed to cow race, lactation stage, and feeding practice, i.e. the use of iodine supplementation. To address this point, we analyzed samples of raw milk that were taken directly from dairy farms all over Switzerland. The sampling was done on a single day in mid September 2007 to exclude seasonal fluctuations. **Figure 5** shows the distribution of iodine in raw milk. The distribution represents a snapshot of milk iodine at a time at which the concentrations begin to increase again to the winter levels, so allowing a comparison of the variability of values between different farms. The mean value (± standard deviation) was 70.4 ± 56.0 µg/l (geometric mean 54.1 µg/l). In addition, a year-round distribution of milk iodine was simulated based on previous data, yielding a considerably higher mean value of 103 ± 38.8 µg/l (geometric mean 96.2 µg/l). The smaller standard deviation reflects the narrower distribution of iodine concentrations in summer milk attributed to the lower iodine content in summer feed rations.

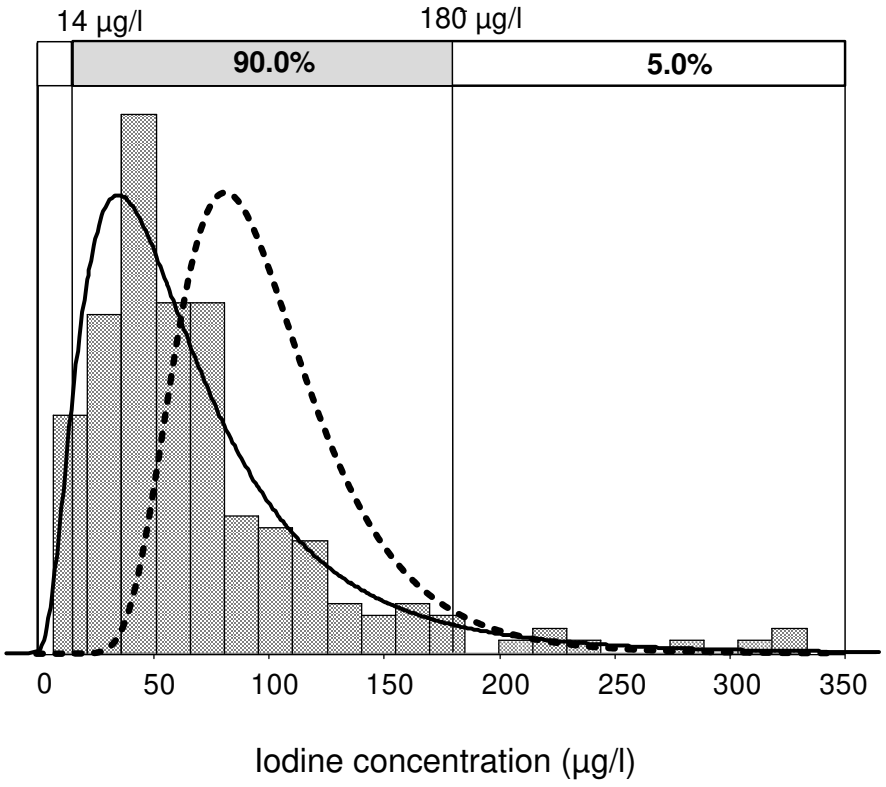

Figure 5: Histogram of iodine concentrations in raw milk sampled directly from Swiss dairy farms on 19th September 2007. The solid line represents the fitted lognormal distribution. The broken line represents a simulated distribution for the year-round iodine milk concentrations based on previous distributions of iodine concentrations (summer and winter), which give both the range of values that the variable could take, and the probability of occurrence of each value within the range.

A post-study evaluation of data provided for a comprehensive milk study (5) was made to assess the influence of milk processing. After adjusting for the effects of season and interaction between milk processing, there were no statistically significant differences between the iodine concentrations of whole and semi-skimmed milk that were either normally pasteurized or ultra-heat treated ($p = 0.589$). There are indications that the amount of iodine in milk has changed significantly in recent years. Compared to the winter-half year value of 1997 (175 ± 79.3 µg/l), milk iodine in recent samples from winter 2011/12 has decreased ($p_{t;\ 0.05} = 0.003$), but still reflecting higher concentrations in winter (**Table 9**). In a comparative study, the contents of iodine in processed milk from nine European countries were measured (25). In the summer half-year, the Swiss iodine concentration in milk was 90.3 ± 14.0 µg/l, which is a value that is higher than previously reported results (on average 30.7 ± 6.7 µg/l) corresponding to the respective period (5). However, according to the European study Switzerland ranked among the countries with the lowest milk iodine levels.

4.5.3 Cheese

For years, the application of iodized salt has been favored to improve dietary iodine supply. Salting is a significant factor in the cheese making process, which is done either by immersing the cheese in brine for some time or by rubbing salt on its surface. The manner in which salt diffuses into the curd mass creates a concentration gradient inside the cheese. The salt penetrates from the outside and progressively reaches the center of the cheese. As time passes, the salt concentration tends to even out; however, depending on the type of cheese a gradient may still persist for an extended period. The diffusibility of iodine as iodide is completely different to that of sodium chloride; iodine is concentrated predominantly in the peripheral layers and the subsequent diffusion to the center can be inhibited by interaction with the proteins of the cheese matrix (26). In a comparative diffusion study with iodized and non-iodized salt, identical hard cheese samples of the Gruyère type were prepared in both ways (6). After a storage and ripening time of seven months, iodine was analyzed from different locations in the cheese wheel: crust, below the crust and center. There was no significant difference in iodine concentration between the two Gruyère samples prepared with iodized and non-iodized salt at the locations below the crust and in the center. Only in the crust itself had iodine accumulated in the Gruyère cheese that was made with iodized salt. It can be concluded that the use of iodized salt in brines has no effect on the iodine concentration of hard cheese. For this reason, it may not be necessary to utilize iodized salt in all hard cheese production processes because consumers normally cut away the crusts. Conversely, soft cheeses such as Camembert show a completely different picture. The application of iodized salt results in a clearly increased cheese iodine concentration, even though a difference in concentration between the peripheral and core layers may still exist.

We monitored the fate of iodine during soft cheese production in all intermediate stages of Camembert production (**Figure 6**). The respective samples were obtained from a producer. The change of the iodine concentration (dry matter) in each step is illustrated in Figure 6. A slight decrease in iodine concentration occurred during the milk thermalization process. However, a large fraction of the milk iodine is lost because it partitions into the whey, which is separated from the protein coagulum. After the raw Camembert was immersed in brine, the iodine concentration rose above the initial milk value. Subsequently, some losses were observed during the ripening period. In addition, the starting milk for

the Emmental making process and the final cheese have been measured. The iodine data are overlaid in Figure 6 showing the fundamental differences between hard and soft cheese production. The iodine concentration in the final cheese is much lower than in the starting product. Apparently, immersion in brine with iodized salt did not have much of an effect on the iodine concentration in the Emmental cheese type. Even though the final salt concentration in Emmental cheese is comparatively low, the measurements confirm the fact iodine does not penetrate deeply into hard cheese. A similar but less extreme pattern of behavior has been observed in half-hard cheese, however, with iodate for brine salting (27).

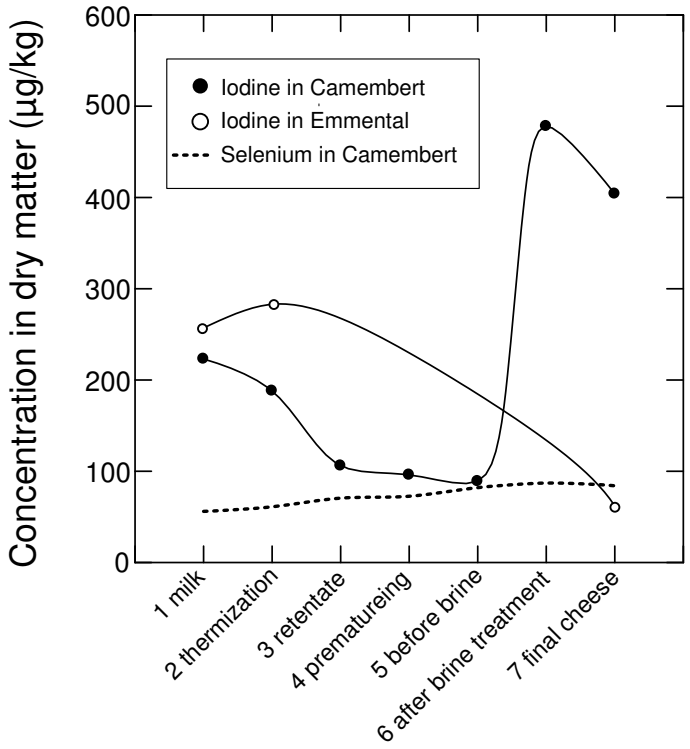

Figure 6: Iodine concentrations in consecutive cheese production stages and the effect of salting with iodized salt. The black dots denote iodine soft cheese (Camembert) and the white dots denote iodine hard cheese (Emmental). The dotted line illustrates the concomitant selenium concentration in the soft cheese production in comparison to iodine.

On the whole, producers no longer use iodized salt, as is illustrated by the decrease of the iodine concentration in the cheese samples from 2011 (**Table 9**). In particular, the iodine levels in hard and semi-hard cheeses were much higher ten years ago. However, the results are in contradiction to the above-mentioned diffusion studies (6;26;27). If the transport mechanism was diffusion, an equilibrium should be established with a constant concentration. Obviously that was not the case as the concentrations were much higher in the outer zones. Moreover, it is unlikely that the high values observed in the year 2000 are due to high milk levels because all of the samples were taken at the same time of year. The protein matrix of cheese is relatively loose and porous. Iodine moves freely along the cheese macro pores, whereby it is also interacting with the bulk material, in which it is trapped in the protein matrix. The ratio between trapped and free iodine depends on the proteins and also on the salt concentration. For this reason, the structure of cheese plays a critical role in the mechanism of iodine transport.

4.6. Food consumption and dietary intakes

A rough estimation of dietary intake for the population can be calculated from food consumption statistics (28) and the reported iodine content of the various food groups (4). A comparison of these data can be seen in **Figure 7**, which shows the average iodine intake superimposed on the values of average iodine content of a particular food group. We can immediately see that the highest contribution to our general diet is from (the salt in) bread, although it itself is not the richest source of iodine. Fish, the highest natural source of iodine contributes far less, but still significantly, to our diet. The average daily intake calculated from food consumption data is approximately 140 µg. It should however be noted, that this value was calculated using the iodine content of foodstuffs as determined by Haldimann et al. in 2005 (4) and it will not be accurate if the iodine content of food has altered over the years. This gives only a general picture for the population as a whole, there is obviously a great variation in the diet from person to person and trends in nutrition are changing all the time. There are differences between the diets of men and women, families and people living alone, families with a stay at home parent and those with working parents etc. Women for example tend to eat more fruit and vegetables than do men (29). An adult following the dietary recommendations of the Swiss Society for Nutrition and the Federal Office of Public Health (30) will have an average daily intake of approximately 145 µg of iodine, which meets the requirements as recommended by the WHO (**Table 10**).

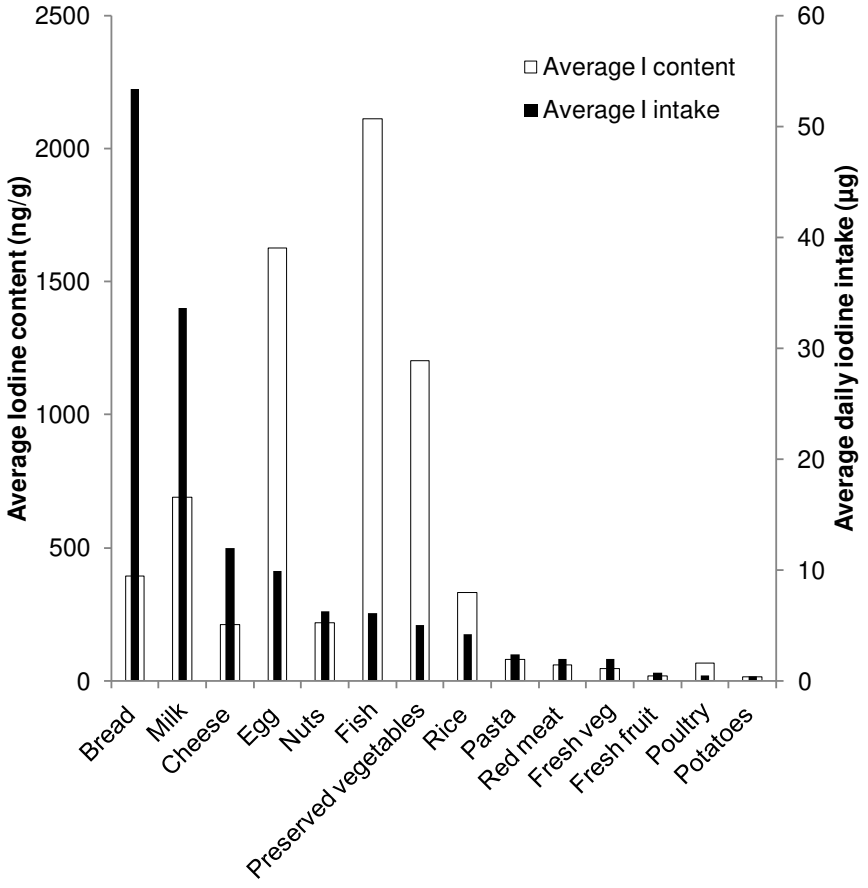

Figure 7: Average iodine content in various food groups and the resulting contribution to the dietary iodine intake.

Table 10: Daily iodine intake calculated from the Table 1 and the recommendations (selection, portion and portion size) for healthy, tasty eating and drinking for adults.

	N° of portions	Portion size (g)	water content (%)	RDA dry weight (g)	Iodine content of food (ng/g)	Iodine per portion (µg)	Total average daily iodine intake (µg)
Fruit/ Vegetables	5						2
3 vegetables	3	120	91	10.8	47	0.5	
2 fruit	2	120	83	20.4	18	0.4	
Starch	3						41
bread		125		125	469	58.6	
pulses		100	91	9	65	0.6	
Potatoes		300	81	57	16	0.9	
pasta		75		75	80	6.0	
rice		75		75	35	2.6	
Protein sources	1						31
fish		120	75	30	2110	63.3	
meat		120	72.5	33	53	1.7	
eggs		157.5	80	31.5	1625	51.2	
fresh cheese		200	55	90	473	42.57	
hard cheese		60	36	38.4	473	18.16	
tofu		120	58	50.4	128	6.45	
Nuts	1	30		30	218	6.54	7
Dairy products	3						64
Milk		200	82	36	690	24.8	
Yoghurt		180	72	50.4	670	33.8	
fresh cheese		200	55	90	211	19.0	
hard cheese		60	36	38.4	205	7.9	
Total							145

The National Health Survey of 2002 shows that 61% of the population eat fish at least once a week, 29% less often and 10% never eat fish. Young people (ages 15-24 years) eat the least, only 50% eat fish once or more a week. Socio-economic group also influences diet. It has been shown that people with a higher level of education and a higher income eat more fish. A geographical difference is also seen between the language regions of Switzerland: 78% of people living in the French-speaking part of the country eat fish once a week compared to 72% in the Italian-speaking region and 56% in the German-speaking regions. Foreigners (71%) eat more fish than do Swiss (59%). From these data, we can conclude, that although fish is a rich source of iodine, there is a significant part of the population for whom this is not the case.

Another statistic that must be treated with care is the amount of milk consumed per person. Again, the survey of 2002 shows polarized attitudes to milk consumption: 36% of the population as a whole drinks milk daily, while 38% never drinks it. However, it should be noted that, in general, children drink much more milk than adults. Men are more likely to drink milk than women. More milk is drunk in rural areas compared to towns and cities. For milk, there is little difference between the language regions. The higher the educational level and income, the less milk is consumed. Other dairy products are consumed daily by the vast majority of the population (98%) and no great difference is seen between men and women (29).

The consumption of fast food, ready meals and processed foods is on the increase. With the increasing numbers of working parents, commute times, and working hours, more and more people are opting to eat from fast-food restaurants or from a limited range of pre-prepared foods. Young people are more likely to opt for such sustenance. 54% of people aged 15-24 years eat fast-food once a week, 32% aged 25-34 years, 19% of 35-44 year olds, dropping to 3% of pensioners (29). Indeed, 8% of the Swiss population states that they never cook (31). The ready meals and ready-made pizzas analyzed show high iodine content (**Table 9**). It should be noted however that these pizzas were sourced from a Swiss bakery and so were made with iodized salt.

4.7. Vegetarianism

As shown in **Table 9**, fish, eggs and dairy products can be good sources of dietary iodine and restricting intake of these can lead to inadequate iodine intake, particularly if the individual does not use iodized salt. The iodine content of plants is dependent on the soil in which the plant grows; in many countries, including Switzerland, this is low and so insufficient iodine is harvested from the diet. A study in Germany showed that people following a strict vegetarian diet are at risk of iodine deficiency and this risk is augmented when iodization of processed foods is restricted due to legislation (32).

4.8. Effects of cooking

There are few studies on the effect of the cooking process on iodine in foods. Iodine loss depends on the type of iodine present in the food. Switzerland for example, uses iodide in iodized salt whilst iodate is preferred in other countries. One study reported the manner of cooking foods (frying, baking or steaming) is largely irrelevant in terms of iodine losses (33), but the amount of iodine lost is dependent on the cooking utensils used and the presence of other ingredients such as reducing sugars, food additives and acidulants. In contrast, studies on meatballs in Poland have shown that iodine loss varies greatly with cooking method. In this study, meatballs were made with iodized salt and by cooking in hot air rather than frying; only 5.5% iodine was lost as compared to 31.7%. Steaming vs. boiling showed losses of 42.9% and 64.9% respectively (34). In another study, a figure of 25.1% is quoted for a loss of iodine from a steamed meatball (35).

The majority of iodized salt used in the home is in boiling water e.g. for the cooking of pasta, rice and potatoes. It has, however, been shown that these foodstuffs do not take up iodine from the water to

any great extent (36). Hence, this is not reliable as a source of iodine in our diets and so increasing the iodine content of salt available in the household will have only a limited effect on increasing iodine levels in the population as a whole. It is the use of iodized salt in processed foods that plays the determining role.

4.9. Recommendations

- Public health recommendations and dietary guidelines now encourage people to reduce their salt intake for cardiovascular health, and this could have a detrimental effect on the iodine levels of the Swiss population, as fortified salt is the main dietary source of iodine. In addition, the use of iodized salt by Swiss households and the food industry is voluntary. Also, changes in industrial practices and trade legislation can reduce dietary iodine supply. For all of these reasons, continued monitoring of iodine concentration in food, together with surveys of the population status, remains necessary in Switzerland.
- The consumption of commercially produced bread is widespread, and is the most important vector for iodine supply in Switzerland. However, bread contains relatively high concentrations of salt and is therefore a target for salt reduction. However, an increase in the salt iodine concentration could compensate for a decrease of the salt content in bread.
- Cheese could be an important nutritional source of iodine in Switzerland. However, the current use of non-iodized salt in its production because of labeling and export issues has reduced its contribution to iodine intakes in the population. Although not feasible for many producers, for cheese that is sold only on the domestic market, iodized salt, labeled as such, should be used instead of common salt.
- Iodized salt consumed from home-cooked food contributes only a small proportion of the total iodine intake since most of salt consumption comes from processed foods. Therefore, it is critical that the Swiss food industry continue to use iodized salt in their products. To achieve this, continued advocacy toward the food industry from the Swiss government and other concerned groups is important.

4.10. References

1. Zimmermann MB. Methods to assess iron and iodine status. British Journal of Nutrition 2008;99:S2-S9.
2. WHO, FAO. Iodine. 2 ed. Vitamin and mineral requirements in human nutrition. Geneva, Switzerland: World Health Organization; Food and Agriculture Organization of the United Nations 2004:303-17.
3. WHO. Iodine Deficiency in Europe:A continuing public health problem. Geneva, Switzerland: World Health Organization, UNICEF, 2007.
4. Haldimann M, Alt A, Blanc A, Blondeau K. Iodine content of food groups. Journal of Food Composition and Analysis 2005;18:461-71.

5. Sieber R, Badertscher R, Bütikofer U, Nick B. Beitrag zur Kenntnis der Zusammensetzung von schweizerischer pasteurisierter und ultrahocherhitzter Milch. Mitteilungen aus Lebensmitteluntersuchung und Hygiene 1999;90:135-44.
6. Goy D, Häni JP, Piccinali P, Wehrmüller K, Jakob E. Das Salz und seine Bedeutung. ALP Forum 2008;59:1-18.
7. Haldimann M, Eastgate A, Zimmerli B. Improved measurement of iodine in food samples using inductively coupled plasma isotope dilution mass spectrometry. Analyst 2000;125:1977-82.
8. Scientific Committee on Food. Opinion of the Scientific Committee on Food on the Tolerable Upper Intake Level of Iodine. SCF/CS/NUT/UPPLEV/26 Final. 2002. European Commission Health & Consumer Protection Directorate-General.
9. Anke M, Groppel B, Angelow L, Elke Scholz J. Der Transport des Jods in der Nahrungskette. In: Haas HJ, ed. Mechanismen des Transports von Mineralstoffen und Spurenelementen. Stuttgart: Wissenschaftliche Verlagsgesellschaft mbH. 1995:1-19.
10. Bogdanov S, Haldimann M, Luginbuhl W, Gallmann P. Minerals in honey: environmental geographical and botanical aspects. Journal of Apicultural Research 2007;46:269-75.
11. Pfammatter, E. Unpublished data from the same study as "Détermination d'arsenic dans l'eau potable". Rapport Annuel, 22-27. 1999. Laboratoire Cantonal du Valais.
12. VSR. Die heutige Situation des jodierten Salzes in der Schweiz. 1978. Schweizerhalle, Vereinigte Schweizerische Rheinsalinen.
13. von Fellenberg Th. Das Vorkommen, der Kreislauf und der Stoffwechsel des Jods. Ergebnisse der Physiologie 1926;25:12-363.
14. Kaufmann S, Wolfram G, Delange F, Rambeck WA. Iodine supplementation of laying hen feed: A supplementary measure to eliminate iodine deficiency in humans? Zeitschrift fur Ernahrungswissenschaft 1998;37:288-93.
15. Wagner V, Windisch W, Swoboda S, Ettle T. Influence of increasing iodine supplementation of feed on growth performance, carcass characteristics and iodine concentration in muscle and liver tissue of fattening pigs. Anwendung und Bedeutung ausgewählter Spurenelemente und Mineralstoffe in der Medizin 2009;3:117.
16. WHO. Trace elements in human nutrition and health. Geneva, Switzerland: World Health Organization, 1996.
17. Fiedlerova V. Spectrophotometric determination of iodine and its content and stability in selected food raw materials and products. Czech Journal of Food Sciences-UZPI 1998;16.
18. Fachschule Richemont. Salzgehalt im Schweizer Brot. Richemont Fachblatt 2009;8-9.
19. Schöne F, Leiterer M, Lebzien P, Bemmann D, Spolders M, Flachowsky G. Iodine concentration of milk in a dose □response stud
iodine intake. Journal of Trace Elements in Medicine and Biology 2009;23:84-92.
20. Flachowsky G, Schone F, Leiterer M, Bemmann D, Spolders M, Lebzien P. Influence of an iodine depletion period and teat dipping in the iodine concentration of serum and milk of cows. Journal of Animal and Feed Sciences 2007;16:18.

21. Busato A, Trachsel P, Schällibaum M, Blum JW. Udder health and risk factors for subclinical mastitis in organic dairy farms in Switzerland. Preventive Veterinary Medicine 2000;44:205-20.

22. Agroscope. Wie viel Jod enthält Milch und wie hoch ist der Übergang von Jodzusätzen aus dem Futter? 2012.

23. Schällibaum M. Saisonale und regionale Schwankungen der Jodkonzentration in den Lieferanten-Milchproben. Schweiz Vereinigung Zuchthyg Buiatrik 1991;103.

24. Schöne F, Lebzien P, Bemmann D, Leiterer M, Spolders M, Flachowsky G. Influence of increasing dietary iodine supplementation of feed on iodine concentration in blood serum and milk of dairy cows. Proc Soc Nutr Physiolog 2006;15:172.

25. Ryšavá L, Kubacková J, Stránský M. Jod und Selengehalte in der Milch aus neun europäischen Ländern. Ernährung/Nutrition 2008;32:65-8.

26. Sieber R. Verwendung von iodiertem Kochsalz bei der Käseherstellung. Ernährung 1998;22:196-201.

27. Hoffmann W, Anke M, Buchheim W. The use of iodized brine for iodine enrichment of semi-hard cheese. Milchwissenschaft 1997;52:257-9.

28. SBV. Nährungsmittelverbrauch pro Kopf. http://www.sbv-usp.ch/de/statistik/ernaehrung/ . 2011. Schweizerischer Bauernverband.

29. Tschannen, A. and Calmonte, R. Resultate zu den Gesundheitsstatistiken in der Schweiz. Ernährungsgewohnheiten in der Schweiz. Stand und Entwicklungen auf der Grundlage der Daten der Schweizerischen Gesundheitsbefragungen 1992, 1997 und 2002. 2005. Neuchâtel, Bundesamt für Statistik.

30. SGE. Recommendations for healthy, tasty eating and drinking for adults. 2009. Berne, Switzerland, Swiss Society for Nutrition.

31. Schaub, A. and Palladino, C. Schlussbericht NANUSS Pilot: Ernährungsverhalten. 2010. Zürich, Switzerland, gfs-zürich, Markt und Sozialforschung.

32. Remer T, Neubert A, Manz F. Increased risk of iodine deficiency with vegetarian nutrition. British Journal of Nutrition 1999;81:45-9.

33. Chavasit V, Malaivongse P, Judprasong K. Study on stability of iodine in iodated salt by use of different cooking model conditions. Journal of Food Composition and Analysis 2002;15:265-76.

34. Waszkowiak K, Szymandera - Buszka K, Witold J, Gorecka D. Comparative evaluation of nutritive and sensory value of selected raw materials and dishes after thermal processing in a convection oven and with conventional methods . Electronic Journal of Polish Agricultural Universities 1999;2:1-8.

35. Waszkowiak K, Szymandera-Buszka K. Effect of collagen preparations used as carriers of potassium iodide on retention of iodine and thiamine during cooking and storage of pork meatballs. Journal of the Science of Food and Agriculture 2007;87:1473-9.

36. Ballauff A, Rost-Reichert I, Kersting M, Weber P, Manz F. Erhöhung der Jodzufurh durch die Zubereitung von Kartoffeln, Nudeln und Reis mit jodiertem Speisesalz. Ernährungs-Umschau 1988;35:16-8.

5. Iodized salt use by the food industry and coordination of public health messages on sodium reduction and iodized salt use

Dr. Maria Andersson

The author declares no conflict of interest.

5.1. Summary

In Switzerland, salt is an effective vehicle for iodine fortification and is a major contributor to dietary iodine needs. Although iodine intake remains adequate in school children and pregnant women, iodine intakes are at the lower end of the optimal range. Moreover, the iodine intake in lactating women and weaning infants in Switzerland is borderline low. Use of iodized salt by households remains high, at greater than 80%, but use of iodized salt in industrially processed foods appears to be decreasing. Because most salt intake in Switzerland comes from processed foods, the use of iodized salt in all processed foods needs to be strongly promoted. The strategy to reduce salt intake is not in contradiction with the salt iodization program; these two important public health policies can be complementary but it is imperative that they be integrated. A reduced salt intake will require adaptations to the present Swiss iodine intervention strategy by: 1) ensuring high penetration rate of iodized salt in food production; and 2) adjusting the iodine fortification levels in salt to compensate for the lower salt intake. Iodine status should be monitored on a regular basis in school age children, pregnant and lactating women and infants. For the latter two groups, if the iodized salt program cannot provide adequate iodine intakes in the future, alternative intervention strategies will need to be considered. An effective iodized salt program in Switzerland that ensures adequate iodine for all age groups will require a joint effort of all partners including the Swiss Federal Office of Public Health, salt industry, food producers, academia, health professionals and consumer organizations.

5.2. Global Perspective

5.2.1 Introduction

The strategy to control iodine deficiency with iodized salt has been remarkably successful, in Switzerland and worldwide. Iodized salt is available in households of 71% of the global population, up from 20% in 1990 (1). Switzerland was one of the pioneer countries to fortify salt with iodine already in 1922 and the Swiss voluntary salt iodization strategy is often used as an exemplary model for other programs (see Chapter 3 of this report) (4, 5). But despite extensive national and global achievements in the control of iodine deficiency, many industrialized countries are lagging behind. More than one third of the iodine deficient countries are in the industrialized part of the world, eleven of them are European (3). In countries like U.K., Australia and New Zealand the iodine intake has deteriorated in the recent years and iodine deficiency reappeared (10-14). This is an apparent paradox as the overall salt intake in most countries steadily increased to levels far above the recommended salt intake (16). Falling iodine intakes is a worrisome trend, indicating that a large proportion of the salt consumed may not be fortified with iodine. Even if iodized salt for household use is available in most industrialized

countries, the food industry is partly reluctant to use iodized salt and much of the salt used in food production is not iodized. A recent study from Germany indicates that decreased iodine status may be attributed to the low use of iodized salt in processed foods (17). This chapter focuses on the importance of the use of iodized salt in the food production to maintain adequate iodine status in industrialized countries. The present situation of iodized salt use by the Swiss food industry and the potential consequences of public health activities for sodium reduction on iodine status in the Swiss population are discussed.

5.2.2 Iodized salt in processed foods

Iodized salt is generally the main dietary source of iodine in the industrialized part of the world (5, 17). WHO recommends salt to be fortified with iodine at a level of 20-40 mg iodine per kg salt, based on an estimated average salt consumption of 5-10 g/day in adult populations (18). Milk and dairy products are other rich dietary iodine sources (19-23), particularly important in children (17, 21, 24, 25) and in countries without iodized salt (25, 26). Salt water fish and seafood have high natural iodine content (27), but their contribution to the overall dietary iodine intake is modest (17, 25). Detailed discussion of the iodine content of Swiss foods can be found in Chapter 4 of this report.

The dietary salt intake in the general population is high (8-12 g/day) in most parts of the world (28) and is 2-3 times the recommended 5 g per day (16, 29, 30). Iodine added to household salt generally used to be the main iodine source at times when most meals were prepared at home. However, the food consumption patterns in industrialized countries have largely changed and discretionary salt added while cooking or eating a meal is now estimated to only 11% of the total salt intake (31). Adults consuming on average ca. 10 g/day have an iodine intake from iodized household salt of about 20-40 µg/day, far below the daily dietary iodine requirement (32, 33).

The main part of the total salt intake comes from salt used in the food production, ready-made foods obtained from a store or a restaurant (16, 31, 34). Foods like bread and processed meat have particularly high salt content and contribute the most (35-37). The salt intake from processed food generally increases with age and tends to be higher for males than females (14, 35, 37-40). The use of iodized salt in the food production is crucial to meet the iodine requirements of the population in industrialized countries. Chapter 4 of this report includes a discussion of the use of iodized salt in Swiss foods. Nevertheless, only few countries mandate salt used in the food industry to be iodized (5, 41, 42). In most countries it is up to the producer to choose whether to use iodized salt in the food production or not. A recent survey among food companies in 39 countries shows that use of iodized salt in the food production varies substantially between countries and between companies within the same country (43). The same is true for foods obtained from a store or a restaurant. A study of iodine content in fast foods in the United States reports that the fast food chain Burger King used iodized salt, whereas McDonald's, Wendy's, and Taco Bell did not (44).

The reason for the reluctance from the food industry to use iodized salt appears to mainly be lack of awareness of the importance of iodine in nutrition and of salt as a fortification vehicle for iodine (43). The hurdle is not primarily cost, as the price difference between iodized and non-iodized salt is negligible in most countries (43). Trade barriers are other reasons for not using iodized salt in the food

production identified by food industry representatives, i.e. some countries prohibit the addition of iodized salt to processed foods, which may impact export (43). Consumers' skepticism about food additives and misconceptions that iodized salt may change taste or color in food products are other constraints. Additional factors listed by the food industry are increased production costs if some foods are produced with iodized salt and other are not, lack of resources and technical capability, lack of enforcement, instability of iodine, potential equipment and process overhauls and competing priorities, although most of these reasons may be of minor importance for food producers in the industrialized world (43).

Despite barriers, there are several good examples of how the food industry can contribute to ensure adequate iodine intakes in the population. Denmark, Australia and New Zealand are now mandating the use of iodized salt in bread production (49-51). In Denmark the law was introduced in 2000 and iodine status is now adequate in the general population (49, 50). In Australia and New Zealand the program was introduced in 2009 and recent local data now indicate that the iodine intake has increased and is adequate (52, 53). In the Netherlands and Belgium, the baking industry use iodized salt on a voluntary basis, enough to maintain adequate iodine intakes of the general population (54, 55).

Information on the iodine content in processed foods is limited. Food packages declare total salt content, but there are no uniform rules for declaring whether iodized salt has been used in the food production. Food composition databases generally contain information on the total salt content of foods, but they rarely specify if the salt used is iodized or not. Even if iodized salt is declared, there may be differences in salt iodine content between brands of the same product or even for the same brand sold in different countries. This makes it difficult to keep food composition databases up-to-date. A large multicenter study is underway to compare the contribution of salt from processed foods between countries, between food companies, and over time (56). Such data should be accompanied with information on the actual use of iodized salt in processed foods.

5.2.3 Salt reduction strategies

Dietary salt reduction initiatives to decrease the salt intake and reduce the risk of heart disease are now being launched around the world (28, 57-59). Consumer education and awareness campaigns are introduced together with activities aiming at the food industry to reduce the total salt content in foods. Salt reduction initiatives do not conflict with salt iodization strategies, if all salt used in food production is iodized and the iodine fortification levels are adapted to the actual average amount of salt consumed (60-62).

The effects of reduced salt intake can be simulated with the help of statistical models (5, 54, 63, 64). Individual level data from food consumption surveys can be used in prediction models to estimate the habitual iodine intake from: 1) native iodine content in foods; 2) iodized salt added to industrially processed foods; 3) discretionarily iodized salt; and 4) iodine containing dietary supplements. The total iodine intake in a population can be estimated and the percentage of the population with adequate intakes can be defined based on the Estimated Average Requirement (EAR) cut-point method (65,

66). The nutrient intake is satisfactory when most individuals of the population (97-98%) meet the EAR, i.e. the acceptable proportion of inadequate intakes is 2-3%.

The anticipated effect by different salt intakes or salt iodine levels can be estimated by varying the amount of salt consumed from different types of foods and altering the market shares of iodized salt-containing industrially processed foods. Such simulation studies have recently been conducted in the Netherlands, New Zealand and Belgium (54, 55, 63, 64). These show that a key factor to maintain adequate and homogeneous iodine intake in the population is to ensure a high use iodized salt in industrially processed foods. The Dutch study demonstrates that even when the salt intake is reduced (by 50%) to the recommended intake level of 5-6 g/d, mandatory use of iodized salt in bread, at the present fortification level of 58 mg/kg salt, and of discretionary salt at a level of 20 mg/kg, maintains adequate iodine intakes in the general population (63). Simulation models like this may be useful when planning the anticipated effects of reductions in salt intake. A limitation with prediction models is that they are largely based on dietary assessment data of and that the total salt intake and the iodine intake from iodized salt may lack precision(67-69).

The recommended fortification levels of 20-40 mg iodine per kg salt levels are safe up to salt intakes of around 25 g/day (70). But, commercially available iodized salt may contain iodine in the range of 15-80 mg iodine per kg salt (5, 41). The optimal window for iodine intakes in the population is relatively narrow. On one side are pregnant and lactating women with high iodine requirements and on the other side stands the risk of high intakes in other subgroups. The individual iodine intake should not exceed 600 µg/day and the population UIC should not exceed 300 µg/L (71, 72). Thus, before adjusting the iodine levels in iodine fortification programs factors such as the foods consumed, salt and iodine food sources, iodine nutritional requirements of the population and vulnerable subpopulations (young children, pregnant and lactating women) have to be considered to ensure iodine intakes which cover all groups and do not pose a risk of high intakes in other groups (60, 62). An Expert Committee convened by the Pan American Health Organization on Optimizing Dietary Salt and Iodine is currently developing a framework for such activities that could serve as model for other countries (62).

5.2.4 Vulnerable population groups

It is unclear whether iodized salt supplies enough dietary iodine for all population groups including pregnant women, lactating women and their breastfed infants with higher iodine requirements (63, 64). In some countries, pregnant and lactating women have low intakes even when SAC and the general population have optimal intakes (73-75). The iodine intake of breastfed infants relies solely on the iodine concentration of breast milk, which, in turn, reflects the mother's iodine status (76). The iodized salt program gets to the infants only indirectly through the breast milk. Lactating women have high iodine requirements due to the iodine transferred to the breast milk and may be at risk of iodine deficiency, despite adequate intakes in the general population (9, 33).

Several countries, with and without iodine deficiency, have recognized this fact and are recommending iodine supplementation to all pregnant and lactating women, e.g. Australia and New Zealand with mild iodine deficiency (77) and the U.S. with overall adequate iodine status (78-80). The recommendations in these countries state that all prenatal vitamin/mineral preparations should contain 150 µg of iodine

and that daily iodine supplementation should continue through lactation (77-80). However, it should also be emphasized that the scientific basis for the recommended daily iodine intake in lactating women and young infants, the criteria to assess their iodine status and the present recommendation to provide targeted iodine supplementation is poor.

In countries with iodized salt as main strategy to control iodine deficiency, attention must also be paid to weaning infants. Infants are at high risk for iodine deficiency, because their iodine requirements per kg body weight are much higher than at any other time in the life cycle (33, 81, 82). Salt and salty foods should be avoided during the first year of life (83). Data on iodine status in weaning infants is limited, but recent studies indicate that the intake may be low, particularly infants not receiving iodine-containing infant formula milk (9, 63, 76, 84). Chapter 3 of this report contains data on the iodine status of Swiss infants and discusses the effects of different feeding practices.

5.2.5 Monitoring

All iodine intervention programs require careful population monitoring of the iodine status, as both iodine deficiency and iodine excess may have adverse health effects. Monitoring of iodine status will become particularly important as salt reduction strategies take effect. Iodine status in the population is monitored by measure UIC in a spot urine sample (72). School-aged children have traditionally been the main age group for iodine surveys, primarily because they are easily accessible through school surveys (3). However,, with modifications in iodine intakes, the focus for monitoring of iodine status should be shifted to also include risk groups like young children, women of reproductive age, pregnant- and lactating women (85). Monitoring should preferably also include periodic assessment of thyroid function (81).

5.3. The situation in Switzerland

5.3.1 Legislation

The Swiss legislation regulates salt sold for human consumption to be iodized on a voluntary basis, including household salt and salt used in the food production (86-88). The federal decree allows iodine fortification in the range of 20-30 mg/kg salt as iodide or iodate (87). Iodized salt has to be clearly labeled on the salt package and the producer may use the health claim “Sufficient iodine intake prevents goiter” (87). It is obligatory to declare the use of iodized salt in processed foods or other food products (87, 88). The policy is regulated on the national level and there is no common European policy.

5.3.2 Household consumption of iodized salt

Three recent national studies conducted in 6-12 years old children, adults (≥15 years), and pregnant women assessed the consumption of iodized salt in Swiss households (9, 89). Iodized salt is used in three out of four homes of school children and pregnant women, but is only used by one third of adults. In the 2009 UIC study in children (n=916) household salt samples were collected in a sub-sample of 266 randomly selected homes and the iodine content was measured (9). Eighty percent (n=213) of samples had iodine concentrations >15 mg/kg and the median (range) iodine concentration

of those samples was 19.8 (15.1-33.0) mg/kg. In the 2009 UIC pregnancy study (n=648) and the 2010-2011 Swiss Salt Survey (SSS) (n=1448) participants were asked to fill out a questionnaire indicating what type(s) of salt they generally use at home (9, 89). The percentage of pregnant women who reported use of iodized salt was 74% (9). In the SSS only 36% reported that the salt they use is iodized and 34% reported that they use non-iodized salt (89). The remaining participants in the SSS used "spicy salt" or did not know what type of salt they have at home. The consumption of iodized salt was 42% in the German-speaking region, higher than participants from the French and Italian regions ($p < 0.001$). The proportion of iodized salt use is surprisingly low, much lower than earlier reported (8). The data should be confirmed in future studies.

5.3.3 Salt production and sales of iodized salt

The leading salt producer in Switzerland is the Schweizer Rheinsalinen AG (Pratteln, Switzerland), a company owned in part by 25 Swiss cantons. The company produces both iodized and non-iodized salt for the domestic and international market. Sales figures from 2011 indicate a worrisome trend with an increasing proportion of the sales of non-iodized common food grade salt, ca. 50% of all salt sold is not iodized, up from 8% in 1986 (Personal communication, Stefan Trachsel, December 2012) (**Figure 8** and **Figure 9**). However, it is not known what proportion of this salt that is actually sold on the Swiss market. It is plausible that a large portion of the total amount of the salt produced is exported to food companies outside Switzerland.

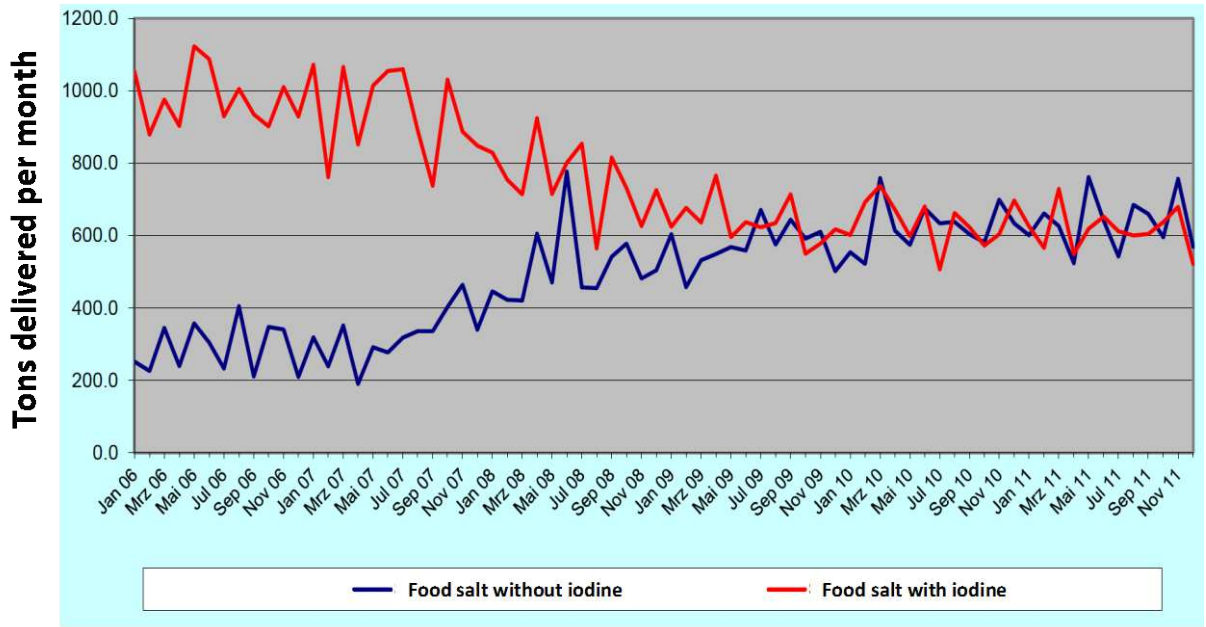

Figure 8: The ratio of iodized vs. not iodized common food grade salt sold in sacks from the Swiss Salt Works has declined over the period 2006-2011.

The overall sale of iodized salt (sold in 0.5 kg, 1 kg, 12.5 kg and 25 kg packages) has been stable over the last 30 years. The total amount of iodized salt sold in cans and smaller packages (0.5 kg and 1 kg), likely mainly for households on the Swiss market, decreased over the last 10 years. Nevertheless, the proportion of the salt sold in small packages that is iodized (out of the total amount

of salt produced) remains stable at 93%. The part of the iodized salt sold in 12.5 kg and 25 kg packages, likely salt sold to restaurants, institutional kitchens, and food producers, has increased 10 fold since the beginning of 1990's. Still, the total amount of iodine used in the overall production went down from 1.36% to 1.11% relative to the total salt production, indicating a decreased overall production of iodized salt.

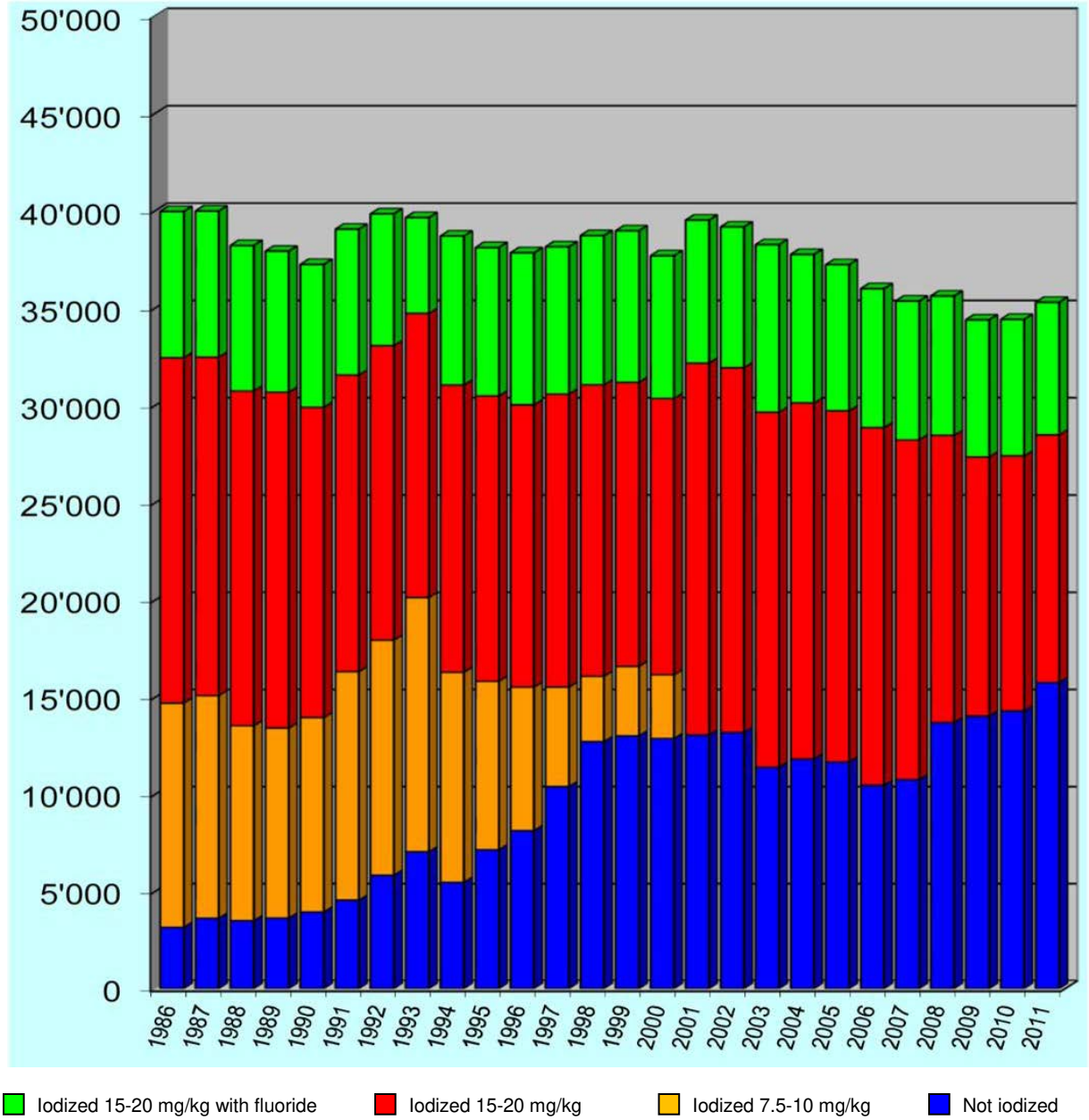

Figure 9: Total sales (tons) of common food grade salt by the Swiss salt works (1996-2011)

5.3.4 Food industry

The Swiss food industry use iodized salt in the food production on a voluntary basis. The information on the iodized salt in processed foods is incomplete and data on the actual penetration rate in Swiss food production is limited. Many cheese producers have discontinued the use of iodized salt, as described in the chapter by Haldiman and Stalder (90).

The reasons for the relatively low use of iodized salt by the Swiss food industry are largely unknown. One reason may be legislative differences between countries in Europe, although the legislation on iodized salt in the neighboring countries Austria, Germany, Italy and France promotes iodized salt for food production (17, 41, 42, 91-93). The legislation in other European countries varies, from no legislation, voluntary to mandatory salt iodization (41). The use of iodized salt by the food industry in Europe is generally low.

5.3.5 Salt intake and coordination of public health messages on salt reduction and iodized salt use

The dietary salt intake in Swiss adults was assessed in a recent nationwide survey of 1448 randomly selected individuals (≥15 years) using 24-hour urine collections (89). The mean (± SD) salt intake was 7.8 ± 3.3 g/24 h in women and 10.6 ± 4.2 g/24 h in men. The intake was clearly above the international recommendation of 5 g/day and only 22% of women and 6% of men had urinary salt excretion below 5 g/24 h. The salt intake appears to have remained at the same level over the past 20 years. A longitudinal study of 13'335 adults (35–74 years) in the Geneva area reports a stable salt intake of 7.8 g/day in women and 10.5 g/day in men over 12 years (1993–2004) (94).

The Swiss Federal Office of Public Health (FOPH) launched a nationwide strategy in 2008 to reduce the dietary salt intake during the 4-year period 2008-2012 (95). The intermediate goal of this strategy is to decrease the overall salt intake to less than 8 g/day by the end of 2012 and the long term goal is to stabilize salt intake to less than 5 g/day (30, 95). Strategies for how to reduce the salt content in processed and restaurant foods were proposed and evaluated in a recent consumer tests study by Zülli and Allemann (96). The investigators propose minimum salt content levels for 4 food categories, i.e. bread and baked goods, meat products, ready-to-serve meals and meal components as well as cheese and cheese products. These food groups, particularly bread, are major iodine sources in the Swiss diet (21, 90, 97). Reduced salt content in the priority food groups may lead to a reduction in the overall iodine intake. However, the information on the proportion of producers using iodized salt in the production of bread, meat products and ready-to-serve meals is limited. The immediate effect of a reduced salt content in these products is therefore difficult to predict unless this information is obtained. Since many cheese producers have discontinued the use of iodized salt (90), a reduced salt content in cheese will likely have small effects on the iodine intake.

The use of iodized salt in the food production should be promoted for all processed foods to minimize the risk of a reduced iodine intake. If all salt used in food production is iodized (at present fortification levels of 20 mg/kg), a salt intake of 8 g/day will meet the iodine requirements of adults (33). Further future reductions in salt intake may require an increase in the iodine fortification level.

International experience from other countries indicates that a salt reduction from currently 9.4 g to 8.0 g per day per person may take longer than the intended 4-year period aimed for by the Swiss Federal Office of Public Health (98). However, a slow reduction in salt consumption and gradual changes in iodine intake is an advantage for population iodine nutrition. Studies from Denmark, where iodine fortification levels were gradually increased in small steps, shows that even small increases in the iodine intake reduces the prevalence of hyperthyroidism in the population, but may still slightly increase the risk of hypothyroidism and thyroid autoimmunity (99-101). The Danish groups

demonstrate that monitoring of thyroid status is an important part of the overall monitoring program for iodine nutrition.

Most Western countries are now launching salt reduction strategies many will face similar issues with regard to iodine nutrition. Exchange of experience between countries will be important. A sustainable reduction of salt consumption and maintained iodine status will be achievable only if all relevant stakeholders, including consumers, cooperate jointly and recognize both public health goals in a combined strategy.

5.3.6 Vulnerable population groups

The most recent Swiss national iodine survey reported 6 and 12 month old infants and their mothers are at risk of low iodine intake (9). (Please see Chapter 3 of this report for more details.) The iodine status of breast-fed infants was lower than in non-breast-fed infants, and weaning infants receiving iodine fortified infant formula had higher median UIC than those who did not. This raises concern that the present iodine intervention strategy may not entirely cover these target groups. Salt reduction strategies without changes in the salt iodine levels may further reduce the already low iodine intake of lactating women. Iodine supplementation to lactating women and iodine fortification of infant formula may therefore be important as an alternative strategy to meet their high iodine requirements.

5.4. Recommendations

- Research: a) Assess the use of iodized salt in the food production; b) Promote food analysis of iodine content in foods; c) Incorporate information on the native iodine content and the iodized salt content in Swiss foods in the Swiss Food Composition Database; d) Adapt the protocol of the upcoming Swiss National Nutrition Survey to incorporate salt and iodine intake so that the dietary data collected can be used in model analysis to predict changes in salt and iodine intake; e) Promote research to define the estimated average requirements for iodine in lactating women and young infants.
- Technical support: a) Technical training and assistance to the food industry in establishing quality control sampling and analytical procedures, if needed.
- Policy: a) Encourage use of iodized salt by the Swiss food industry; b) Promote declaration of iodized salt on food packages; c) Regularly evaluate the data on iodine intake, salt intake, iodine status and thyroid function obtained from the population monitoring to adjust the iodine levels in salt based on the population's intake patterns if needed; d) Ensure appropriate iodine intakes in vulnerable groups, i.e. infants, pregnant women and lactating women; e) Evaluate the need for iodine supplementation of pregnant and lactating women.
- Political commitment and legislation: a) Ensure that policy changes on iodized salt are done in close collaboration with Swiss Fluoride and Iodine Commission; b) Support coordinated European efforts to raise the priority of iodine nutrition on the political agenda in Europe and support a common EU policy for the voluntary use of iodized salt by the food industry, including the cheese-making industry.

- Partnership: a) Ensure continued participation of government partners, national agencies, nongovernmental organizations, salt producers, academia and the health-care sector in the Swiss Fluoride and Iodine Commission and; b) Give the Swiss Fluoride and Iodine Commission continued mandate to review information from monitoring activities for planning and promotion of collaborative work between the different sectors; c) Consider participation of food industry and consumer organizations.
- Advocacy and communication: a) Promote the use of iodized salt in the food production and the households; b) Develop appropriate communication through mass media, the health system, food industry organizations, and other context specific channels to educate the public, salt producers and food producers about the importance of iodine nutrition and salt as a fortificant for iodine; c) Provide support to the Schweizer Rheinsalinen AG to increase the demand of iodized salt from the food industry; d) Information campaigns of iodine nutrition should be combined with and integrated in salt reduction campaigns; e) Advocacy should combine messages on the benefits of salt reduction and adequate iodine intake; f) Potential critics from the public and the food industry should be anticipated and addressed before launching campaigns.
- Monitoring: a) Maintain monitoring and control systems for food at the Cantonal level to ensure adequate salt iodine levels from salt production, food production to consumption; b) Maintain the periodic monitoring of iodine status (UIC) and thyroid function (thyroglobulin concentration) in school children and pregnant women; d) Maintain the neonatal TSH screening program; e) Introduce monitoring systems for assessing iodine status in vulnerable population groups, i.e. infants, women of reproductive age and lactating women.

5.5. References

1. UNICEF. The State of the World's Children 2012: Children in an urban world. New York, NY: United Nations Children's Fund 2012.
2. WHO, UNICEF, ICCIDD. Global prevalence of iodine deficiency disorders. Micronutrient Deficiency Information System working paper 1. Geneva: World Health Organization, 1993.
3. Andersson M, Karumbunathan V, Zimmermann MB. Global iodine status in 2011 and trends over the past decade. J Nutr 2012;142(4):744-50.
4. Zimmermann MB. Research on iodine deficiency and goiter in the 19th and early 20th centuries. J Nutr 2008;138(11):2060-3.
5. Charlton K, Skeaff S. Iodine fortification: why, when, what, how, and who? Curr Opin Clin Nutr Metab Care 2011;14(6):618-24.
6. Bürgi H. Epidemiology and history of iodine nutrition in Switzerland. In: Zimmermann MB, ed. Expertenbericht zur Jodversorgung in der Schweiz. Bern Bundesamt für Gesundheit (BAG), 2012.
7. Hess SY, Zimmermann MB, Torresani T, Burgi H, Hurrell RF. Monitoring the adequacy of salt iodization in Switzerland: a national study of school children and pregnant women. Eur J Clin

Nutr 2001;55(3):162-6.

8. Zimmermann MB, Aeberli I, Torresani T, Burgi H. Increasing the iodine concentration in the Swiss iodized salt program markedly improved iodine status in pregnant women and children: a 5-y prospective national study. Am J Clin Nutr 2005;82(2):388-92.
9. Andersson M, Aeberli I, Wust N, et al. The Swiss iodized salt program provides adequate iodine for school children and pregnant women, but weaning infants not receiving iodine-containing complementary foods as well as their mothers are iodine deficient. J Clin Endocrinol Metab 2010;95(12):5217-24.
10. Vanderpump MP, Lazarus JH, Smyth PP, et al. Iodine status of UK schoolgirls: a cross-sectional survey. Lancet 2011;377(9782):2007-12.
11. Li M, Eastman CJ, Waite KV, et al. Are Australian children iodine deficient? Results of the Australian National Iodine Nutrition Study. Med J Aust 2006;184(4):165-9 (See correction: Med J Aust 2008;188 (11):674).
12. Li M, Eastman CJ, Waite KV, et al. Erratum: Are Australian children iodine deficient? Results of the Australian National Iodine Nutrition Study. Med J Aust 2008;188(11):674.
13. Parnell W, Scragg R, Wilson N, Schaaf D, Fitzgerald E. NZ Food NZ Children: key results of the 2002 national children's nutrition survey. Wellington: Ministry of Health of New Zealand, 2003.
14. Thomson BM, Vannoort RW, Haslemore RM. Dietary exposure and trends of exposure to nutrient elements iodine, iron, selenium and sodium from the 2003-4 New Zealand Total Diet Survey. Br J Nutr 2008;99(3):614-25.
15. Zimmermann MB, Andersson M. Assessment of iodine nutrition in populations: past, present, and future. Nutr Rev 2012;70(10):553-70.
16. Brown IJ, Tzoulaki I, Candeias V, Elliott P. Salt intakes around the world: implications for public health. Int J Epidemiol 2009;38(3):791-813.
17. Johner SA, Gunther AL, Remer T. Current trends of 24-h urinary iodine excretion in German schoolchildren and the importance of iodised salt in processed foods. Br J Nutr 2011;106(11):1749-56.
18. WHO, UNICEF, ICCIDD. Recommended iodine levels in salt and guidelines for monitoring their adequacy and effectiveness. (WHO/NUT/96.13). Geneva: World Health Organization, 1996.
19. Dahl L, Opsahl JA, Meltzer HM, Julshamn K. Iodine concentration in Norwegian milk and dairy products. Br J Nutr 2003;90(3):679-85. doi: S0007114503001740 [pii].
20. Pearce EN, Pino S, He X, Bazrafshan HR, Lee SL, Braverman LE. Sources of dietary iodine: bread, cows' milk, and infant formula in the Boston area. J Clin Endocrinol Metab 2004;89(7):3421-4.
21. Haldimann M, Alt A, Blanc A, Blondeau K. Iodine content of food groups. J Food Compos Anal 2005;18(6):461-71.
22. Li M, Waite KV, Ma G, Eastman CJ. Declining iodine content of milk and re-emergence of

iodine deficiency in Australia. Med J Aust 2006;184(6):307.

23. Schone F, Leiterer M, Lebzien P, Bemmann D, Spolders M, Flachowsky G. Iodine concentration of milk in a dose-response study with dairy cows and implications for consumer iodine intake. J Trace Elem Med Biol 2009;23(2):84-92.

24. Caldwell KL, Makhmudov A, Ely E, Jones RL, Wang RY. Iodine status of the U.S. population, National Health and Nutrition Examination Survey, 2005-2006 and 2007-2008. Thyroid 2011;21(4):419-27.

25. Dahl L, Johansson L, Julshamn K, Meltzer HM. The iodine content of Norwegian foods and diets. Public Health Nutr 2004;7(4):569-76.

26. Bath SC, Button S, Rayman MP. Iodine concentration of organic and conventional milk: implications for iodine intake. Br J Nutr 2011:1-6.

27. Julshamn K, Dahl L, Eckhoff K. Determination of iodine in seafood by inductively coupled plasma/mass spectrometry. J AOAC Int 2001;84(6):1976-83.

28. Webster JL, Dunford EK, Hawkes C, Neal BC. Salt reduction initiatives around the world. J Hypertens 2011;29(6):1043-50.

29. Centers for Disease Control and Prevention (CDC). Usual sodium intakes compared with current dietary guidelines --- United States, 2005-2008. MMWR Morb Mortal Wkly Rep 2011;60(41):1413-7.

30. World Health Organization. Diet, nutrition and the prevention of chronic diseases. Report of a Joint WHO/FAO expert consultation Geneva, World Health Organization, 28 January - 1 February 2002. WHO Technical Report Series 916. Geneva: World Health Organization, 2003.

31. Mattes RD, Donnelly D. Relative contributions of dietary sodium sources. J Am Coll Nutr 1991;10(4):383-93.

32. D-A-CH, Deutsche Gesellschaft für Ernährung (DGE), Österreichische Gesellschaft für Ernährung (ÖGE), Schweizerische Gesellschaft für Ernährung (SGE), Schweizerische Vereinigung für Ernährung (SVE). D-A-CH-Referenzwerte für die Nährstoffzufuhr. Frankfurt am Main: Umschau/Braus Verlag, 2008.

33. Institute of Medicine, Academy of Sciences, USA. Dietary reference intakes for vitamin A, vitamin K, arsenic, boron, chromium, copper, iodine, iron, manganese, molybdenum, nickel, silicon, vanadium and zinc. Washington DC: National Academy Press, 2001.

34. Institute of Medicine. Strategies to reduce sodium intake in the United States. Washington DC: The National Academies Press, 2010.

35. Thomson BM. Nutritional modelling: distributions of salt intake from processed foods in New Zealand. Br J Nutr 2009;102(5):757-65.

36. Ni Mhurchu C, Capelin C, Dunford EK, Webster JL, Neal BC, Jebb SA. Sodium content of processed foods in the United Kingdom: analysis of 44,000 foods purchased by 21,000 households. Am J Clin Nutr 2011;93(3):594-600.

37. Centers for Disease Control and Prevention (CDC). Vital signs: food categories contributing the most to sodium consumption - United States, 2007-2008. MMWR Morb Mortal Wkly Rep

2012;61:92-8.

38. Egan SK, Tao SS, Pennington JA, Bolger PM. US Food and Drug Administration's Total Diet Study: intake of nutritional and toxic elements, 1991-96. Food Addit Contam 2002;19(2):103-25.

39. He FJ, Marrero NM, Macgregor GA. Salt and blood pressure in children and adolescents. J Hum Hypertens 2008;22(1):4-11.

40. Reinivuo H, Valsta LM, Laatikainen T, Tuomilehto J, Pietinen P. Sodium in the Finnish diet: II trends in dietary sodium intake and comparison between intake and 24-h excretion of sodium. Eur J Clin Nutr 2006;60(10):1160-7.

41. World Health Organization. Iodine Deficiency in Europe: A Continuing Public Health Problem Edtion ed. In: Andersson M, de Benoist B, Darnton-Hill I, Delange F, eds. Geneva: World Health Organization, 2007.

42. Zimmermann MB. Symposium on 'Geographical and geological influences on nutrition': Iodine deficiency in industrialised countries. Proc Nutr Soc 2010;69(1):133-43.

43. Ohlhorst SD, Slavin M, Bhide JM, Bugusu B. Use of Iodized Salt in Processed Foods in Select Countries Around the World and the Role of Food Processors. Compr Rev Food Sci F 2012;11(2):233-84.

44. Lee SY, Leung AM, He X, Braverman LE, Pearce EN. Iodine content in fast foods: comparison between two fast-food chains in the United States. Endocr Pract 2010;16(6):1071-2.

45. Winger RJ, Konig J, House DA. Technological issues associated with iodine fortification of foods. Trends Food Sci Tech 2008;19(2):94-101.

46. Longvah T, Toteja GS, Bulliyya G, et al. Stability of added iodine in different Indian cooking processes. Food Chem 2012;130(4):953-9.

47. Thomson BM. Stability of added iodine in processed cereal foods. Food Addit Contam Part A Chem Anal Control Expo Risk Assess 2009;26(1):25-31.

48. Kuhajek EJ, Fiedelma.Hw. Nutritional Iodine in Processed Foods. Food Technol-Chicago 1973;27(1):52-3.

49. Rasmussen LB, Ovesen L, Christensen T, et al. Iodine content in bread and salt in Denmark after iodization and the influence on iodine intake. Int J Food Sci Nutr 2007;58(3):231-9.

50. Rasmussen LB, Carle A, Jorgensen T, et al. Iodine intake before and after mandatory iodization in Denmark: results from the Danish Investigation of Iodine Intake and Thyroid Diseases (DanThyr) study. Br J Nutr 2008:1-8.

51. Food Standards Australia New Zealand. Australia New Zealand Food Standards Code - Standard 2.1.1 - Cereals and Cereal Products - F2009C00811. Prepared 13 Aug 2009. Available at: http://www.comlaw.gov.au/Details/F2009C00811 (Accessed on 2 May 2012). 2009.

52. Ma G, Trieu A, Eastman CJ. Mandatory fortification of bread with iodized salt - A public health success story. Med J Aust 2012;In press.

53. Skeaff SA, Lonsdale-Cooper E. Mandatory fortification of bread with iodised salt modestly improves iodine status in schoolchildren. Br J Nutr 2012:1-5.

54. Verkaik-Kloosterman J, van 't Veer P, Ocke MC. Simulation model accurately estimates total dietary iodine intake. J Nutr 2009;139(7):1419-25.

55. Vandevijvere S, Mourri Bensouda A, Amsalkhir S, Avni F, Van Oyen H, Moreno-Reyes R. Fortification of bread with iodized salt corrected iodine deficiency in school-aged children, but not in their mothers: a national cross-sectional survey in Belgium. Thyroid 2012; 22(10):1046-53.

56. Dunford E, Webster J, Metzler AB, et al. International collaborative project to compare and monitor the nutritional composition of processed foods. Eur J Cardiovasc Prev Rehabil 2011.

57. World Health Organization. Reducing salt intake in populations: report of a WHO forum and technical meeting, 5-7 October 2006 Paris, France. Available at: www.who.int/dietphysicalactivity/reducingsaltintake_EN.pdf. Geneva: World Health Organization, 2007.

58. Legetic B, Campbell N. Reducing salt intake in the Americas: Pan American Health Organization actions. J Health Commun 2011;16 Suppl 2:37-48.

59. Centers for Disease Control and Prevention (CDC). CDC grand rounds: dietary sodium reduction - time for choice. MMWR Morb Mortal Wkly Rep 2012;61(5):89-91.

60. World Health Organization. Salt as a vehicle for fortification. Report of a WHO expert consultation. Geneva: World Health Organization, 2008:1-27.

61. Zimmermann MB. Iodine deficiency in industrialized countries. Clin Endocrinol (Oxf) 2011;75(3):287-8.

62. Campbell N, Dary O, Cappuccio FP, Neufeld LM, Harding KB, Zimmermann MB. Collaboration to optimize dietary intakes of salt and iodine: a critical but overlooked public health issue. Bull World Health Organ 2012;90(1):73-4.

63. Verkaik-Kloosterman J, van 't Veer P, Ocke MC. Reduction of salt: will iodine intake remain adequate in The Netherlands? Br J Nutr 2010;104(11):1712-8.

64. Schiess S, Cressey PJ, Thomson BM. Predictive modelling of interventions to improve iodine intake in New Zealand. Public Health Nutr 2012:1-9.

65. Food and Nutrition Board, Institute of Medicine. Dietary reference intakes: applications in dietary planning. Washington DC: National Academy Press, 2003.

66. Murphy SP, Barr SI. Practice paper of the American Dietetic Association: using the Dietary Reference Intakes. J Am Diet Assoc 2011;111(5):762-70.

67. Bentley B. A review of methods to measure dietary sodium intake. J Cardiovasc Nurs 2006;21(1):63-7.

68. Leung AM, Braverman LE, Pearce EN. A dietary iodine questionnaire: correlation with urinary iodine and food diaries. Thyroid 2007;17(8):755-62.

69. WHO/PAHO Regional Expert Group for Cardiovascular Disease Prevention through

Population-wide Dietary Salt Reduction. A review of methods to determine the main sources of salt in the diet. Available at http://new.paho.org/hq/index.php?option=com_content&task=view&id=2015&Itemid=1757. Accessed on March 13, 2012.

70. World Health Organization. Safe use of iodized oil to prevent iodine deficiency in pregnant women. A statement by the World Health Organization. Bull World Health Organ 1996;74:1-3.

71. EFSA. Tolerable upper intake levels for vitamins and minerals. Available at http://www.efsa.europa.eu/en/ndatopics/docs/ndatolerableuil.pdf. Accessed 2 April 2012. Parma, Italy: European Food Safety Authority, 2006.

72. World Health Organization, United Nations Children's Fund, International Council for the Control of Iodine Deficiency Disorders. Assessment of iodine deficiency disorders and monitoring their elimination. A guide for programme managers, 3rd edition. Geneva: World Health Organization, 2007.

73. Gowachirapant S, Winichagoon P, Wyss L, et al. Urinary iodine concentrations indicate iodine deficiency in pregnant thai women but iodine sufficiency in their school-aged children. J Nutr 2009;139(6):1169-72.

74. Wong EM, Sullivan KM, Perrine CG, Rogers LM, Peña-Rosas JP. Comparison of median urinary iodine concentration as an indicator of iodine status among pregnant women, school-age children, and nonpregnant women. Food and Nutrition Bulletin 2011;32(3):206-12.

75. Ordookhani A, Pearce EN, Hedayati M, et al. Assessment of thyroid function and urinary and breast milk iodine concentrations in healthy newborns and their mothers in Tehran. Clin Endocrinol (Oxf) 2007;67(2):175-9.

76. Mulrine HM, Skeaff SA, Ferguson EL, Gray AR, Valeix P. Breast-milk iodine concentration declines over the first 6 mo postpartum in iodine-deficient women. Am J Clin Nutr 2010;92(4):849-56.

77. National Health and Medical Research Council (NHMRC). Iodine supplementation for pregnant and breastfeeding women. Edtion ed. NHMRC Public Statement, January 2010 Available at: http://wwwnhmrcgovau/_files_nhmrc/file/publications/synopses/new45_statementpdf (Accessed 10 August 2012), 2010.

78. Becker DV, Braverman LE, Delange F, et al. Iodine supplementation for pregnancy and lactation-United States and Canada: recommendations of the American Thyroid Association. Thyroid 2006;16(10):949-51.

79. Stagnaro-Green A, Abalovich M, Alexander E, et al. Guidelines of the American Thyroid Association for the diagnosis and management of thyroid disease during pregnancy and postpartum. Thyroid 2011;21(10):1081-125.

80. Obican SG, Jahnke GD, Soldin OP, Scialli AR. Teratology public affairs committee position paper: Iodine deficiency in pregnancy. Birth Defects Res A Clin Mol Teratol 2012;94(9):677-82.

81. Zimmermann MB. Iodine Deficiency. Endocr Rev 2009;30(4):376-408.

82. Zimmermann MB, Jooste PL, Pandav CS. Iodine-deficiency disorders. Lancet 2008;372(9645):1251-62.

83. Ernährungskommission der Schweizerischen Gesellschaft für Pädiatrie, Baehler P, Baenziger O, et al. Empfehlungen für die Säuglingsernährung 2008. Paediatrica 2008;19(1):19-21.

84. Skeaff SA, Ferguson EL, McKenzie JE, Valeix P, Gibson RS, Thomson CD. Are breast-fed infants and toddlers in New Zealand at risk of iodine deficiency? Nutrition 2005;21(3):325-31.

85. Andersson M, de Benoist B, Delange F, Zupan J. Prevention and control of iodine deficiency in pregnant and lactating women and in children less than 2-years-old: conclusions and recommendations of the Technical Consultation. Public Health Nutr 2007;10(12A):1606-11.

86. Bürgi H. The Swiss legislation on iodized salt. IDD Newsletter 1999;Nov:57-8.

87. Das Eidgenössische Departement des Innern (EDI). Verordnung des EDI über den Zusatz essenzieller oder physiologisch nützlicher Stoffe zu Lebensmitteln vom 23. November 2005 (Stand am 1. November 2010), Art 5 and 6, 817.022.32,. Available at: http://www.admin.ch/ch/d/sr/8/817.022.32.de.pdf. Accessed on 12 Dec 2012.

88. Das Eidgenössische Departement des Innern (EDI). Verordnung des EDI über die Kennzeichnung und Anpreisung von Lebensmitteln (LKV). vom 23. November 2005 (Stand am 1. Januar 2012), Art. 5a, 817.022.21.. Available at: http://www.admin.ch/ch/d/sr/8/817.022.21.de.pdf. Accessed on 12 Dec 2012.

89. Chappuis A, Bochud M, Glatz N, Vuistiner P, Paccaud F, Burnier M. Swiss survey on salt intake: main results: Service de Néphrologie et Institut Universitaire de Médecine Sociale et Préventive, Centre Hospitalier Universitaire Vaudois (CHUV), Lausanne, Switzerland, 2011.

90. Haldimann M, Stalder E. Sources of iodine in Swiss diets. In: Zimmermann MB, ed. Expertenbericht zur Jodversorgung in der Schweiz. Bern: Bundesamt für Gesundheit (BAG), 2012.

91. Weissel M. Legal augmentation of iodine content in table salt from 10 to 20 mg KI/kg: documented effects a decade later. Exp Clin Endocrinol Diabetes 2003;111(4):187-90.

92. Thamm M, Ellert U, Thierfelder W, Liesenkötter KP, Völzke H. Jodversorgung in Deutschland. Ergebnisse des Jodmonitorings im Kinderund Jugendgesundheitssurvey (KiGGS). Bundesgesundheitsbl - Gesundheitsforsch - Gesundheitsschutz 2007;50:744-49.

93. Valeix P, Zarebska M, Preziosi P, Galan P, Pelletier B, Hercberg S. Iodine deficiency in France. Lancet 1999;353(9166):1766-7.

94. Beer-Borst S, Costanza MC, Pechere-Bertschi A, Morabia A. Twelve-year trends and correlates of dietary salt intakes for the general adult population of Geneva, Switzerland. Eur J Clin Nutr 2009;63(2):155-64.

95. Eidgenössisches Departement des Innern EDI, Bundesamt für Gesundheit BAG, Direktionsbereich Verbraucherschutz. Salz Strategie 2008-2012. Strategiepapier zur Reduktion des Kochsalzkonsums. Available at: http://www.bag.admin.ch/themen/ernaehrung_bewegung/05207/05216/index.html?lang=de.

Accessed on 8 May 2012. 2009.

96. Zülli S, Allemann C. Reduktion des Salzkonsums: Reduktion des Salzgehalts in verarbeiteten Lebensmitteln [Reducing salt consumption: Reducing the salt content in processed foods]. Zollikofen: Schweizerische Hochschule für Landwirtschaft SHL, Food Science & Management, 2011.

97. Als C, Haldimann M, Burgi E, Donati F, Gerber H, Zimmerli B. Swiss pilot study of individual seasonal fluctuations of urinary iodine concentration over two years: is age-dependency linked to the major source of dietary iodine? Eur J Clin Nutr 2003;57(5):636-46.

98. Appel LJ, Angell SY, Cobb LK, et al. Population-wide sodium reduction: the bumpy road from evidence to policy. Ann Epidemiol 2012;22(6):417-25.

99. Vejbjerg P, Knudsen N, Perrild H, et al. Lower prevalence of mild hyperthyroidism related to a higher iodine intake in the population: prospective study of a mandatory iodization programme. Clin Endocrinol (Oxf) 2009;71(3):440-5.

100. 100. Pedersen IB, Knudsen N, Carle A, et al. A cautious iodization programme bringing iodine intake to a low recommended level is associated with an increase in the prevalence of thyroid autoantibodies in the population. Clin Endocrinol 2011;75(1):120-6.

101. Andersen S, Iversen F, Terpling S, Pedersen KM, Gustenhoff P, Laurberg P. Iodine deficiency influences thyroid autoimmunity in old age--a comparative population-based study. Maturitas 2012;71(1):39-43.