Thiocyanate in Food and Iodine in Milk: From Domestic Animal Feeding to Improved Understanding of Cretinism

Peter Laurberg,1 Stig Andersen,1 Nils Knudsen,3,4 Lars Ovesen,5 Susanne B. Nøhr,2 and Inge Bülow Pedersen1

Transport of iodine in the mammary gland into breast milk plays a central role in various fields of prevention of thyroid diseases. First, a sufficient content of iodine in the mother’s milk is necessary for normal brain development in the breastfed child. This is attained by expression during lactation in the mammary gland of the sodium iodide symporter (NIS), also responsible for iodine transport in the thyroid. Milk iodine content varies with the iodine intake of the mother, and urinary iodine excretion in groups of mothers seems to be a valuable indicator of the iodine status of their breastfed children. Second, iodine in dairy products provides a considerable part of iodine intake in many populations. Thiocyanate from rapeseed feeding of cows decreases milk iodine content, probably by competitive inhibition of NIS in the mammary gland. Alterations in feeding of dairy cows may alter the iodine content of consumer milk, and this may influence the risk of thyroid diseases in the population. Thiocyanate inhibition of iodine transport into milk may also be operative in humans with a high thiocyanate intake. This could further impair iodine status in breastfed children in low-iodine intake areas of the world. It can be speculated that a low-iodine content of mother’s milk because of inhibition of NIS in the mammary gland may be one factor of importance for development of myxedematous cretinism.

Introduction

OPTIMAL IODINE INTAKE OF A population is pivotal for prevention of thyroid disorders (1). In many countries dairy products contribute considerably to iodine intake (2,3). Therefore, knowledge of factors affecting milk iodine content is important when monitoring population iodine intake. Such knowledge is also central in the efforts to provide small children with optimal amounts of iodine during the period of breastfeeding.

Iodine in Milk

It has been known for many years that the mammary gland is able to concentrate iodine and excrete it into milk (4,5; for an updated review see Semka and Delange [6]). More recently, it has been demonstrated that the main iodide transporter in the mammary gland is the sodium iodide symporter (NIS) also responsible for iodine transport over the basolateral membrane of the thyroid follicular cells (7,8). NIS is expressed in the mammary gland during lactation (9). Most of the iodine concentrated in the mammary gland is present in milk as iodide (10).

The regulation of iodine transport into milk is only partly known. Within certain limits the iodide concentration of milk seems to vary much in parallel with the iodine intake of the mother as shown in Figure 1. The left part of the figure shows the association between iodide concentrations in urine and iodide concentrations of milk in a sample of Danish women day 5 after uncomplicated pregnancy and delivery (11). The right part of the figure shows the importance of milk iodine contents for the iodine status of the newborns as measured by their iodide concentrations in urine in the same study.

The level of iodine in maternal urine was similar to the level in milk (ratio of maternal milk to maternal urine iodide concentration: median, 0.96 [25–75 centiles: 0.50–1.96; n = 142]). The iodide concentrations were also similar in urine from the child and in milk from the mother (ratio of child urine to maternal milk iodide concentration: median, 1.00 [0.60–1.64; n = 137]) and in urine from the child and urine from the mother (ratio of child urine to mother’s urine iodide concentration: median, 1.00 [0.65–1.75, n = 141]). The data illustrate that in a group of women, the average iodide concentration in urine from the mothers is a good measure of the average iodine status of the breastfed children. Such data enable the prediction of the average level of milk iodine from the iodine intake. If average daily milk production is 0.8 L and average urine volume is 1.2 L, then 200 μg of iodine in diet per day will give an average milk iodide concentra-

1Department of Endocrinology and Medicine, 2Department of Obstetrics and Gynaecology, Aalborg Hospital, Aalborg, Denmark.
3Centre for Preventive Medicine, Glostrup Hospital, Copenhagen, Denmark.
4Department of Medicine I, Bispebjerg Hospital, Copenhagen, Denmark.
5Institute of Food Research and Nutrition, The Danish Food Administration, Copenhagen, Denmark.
tion of 90 μg/L if it is assumed that 10% of iodine in diet is excreted in feces.

Studies from Korea with a high iodine intake of lactating mothers show that under such circumstances, milk iodine excretion increases to high levels (12). Use of iodine-containing contrast agents in mothers has also been found to profoundly increase iodine excretion in milk (13). Colostrum contains more iodine than mature milk both in humans (14) and in farm animals (15).

Because various chemicals and natural compounds may inhibit NIS (16) it is interesting to study how intake of such compounds may alter milk iodine content. It has been found that both perchlorate and thiocyanate decrease milk iodine excretion (4). In line with this, abundant studies in veterinary research have shown that thiocyanate from feeding may profoundly alter milk iodine content.

**Rapeseed and Thiocyanate**

Rape (*Brassica napus*) is a 60–100-cm high plant with yellow flowers, belonging to the Cruciferae family. It is widely grown in many countries because the seeds contain 30%–45% of oil. In addition, rapeseed contains high levels of protein. Rapeseed meal or press-cakes are used for feeding animals as a substitute for soybean proteins.

A problem with rapeseed as a protein source is that it contains considerable amounts of glucosinolates, also known as thio glucosides. These are natural, bioactive, sulfur-containing phytochemicals also found in other Cruciferae such as broccoli, brussels sprouts, cauliflower, cabbage, and kale (17). Glucosinolates seem to have cancer-preventive properties (18) but in higher amounts may show a number of toxicologic effects. Potential harmful effects were already reported

![FIG. 1.](image1.png)  
**FIG. 1.** Correlation between iodine contents of mother’s urine and breast milk (left panel, n = 142, Spearman’s ρ = 0.36, p < 0.001) and between iodine in breast milk and child’s urine (right panel, n = 137, Spearman’s ρ = 0.58, p < 0.001) in a cohort of mothers and their newborns after uncomplicated pregnancy and delivery. Participants were random normal pregnant women admitted for labor in hospital clinics in five Danish cities. Nearly all mothers (93%) had taken vitamin/mineral supplements during pregnancy, and this continued after delivery. By chance 36% took supplements containing iodine (150 μg per tablet). Sampling was performed day 5 after delivery but was not fixed to any given time of day. Data from Nøhr et al. (11).

![FIG. 2.](image2.png)  
**FIG. 2.** Effect of rapeseed meal on milk iodine content of cows. Fifteen Holstein-Frisian cows were stratified according to milk yield, and randomly assigned to three grain mixtures fortified with soybean meal (white columns) or Tower (light grey columns) or Turret rapeseed meal (dark grey columns). The trial was divided in three periods (I, II, III) that lasted 2, 8, and 2 weeks, respectively. In periods I and III, all cows received soybean meal while in period II they received the assigned treatments. There was no difference between groups in food volume and iodine intake (mean iodine intake from feeding and water is shown in left panel of figure) and no difference in milk yield. Mean milk iodine content (right panel of figure) was drastically reduced during feeding with rapeseed meal (*p < 0.01 vs. soybean). Data from Papas et al. (23).
in animals in 1928, when rabbits fed large amounts of cabbage developed goiter (19).

Feeding high levels of glucosinolates leads to impaired growth and general health of the animals, which is probably not solely related to altered thyroid function (20). At lower levels of intake, interference with iodine transport and thyroid function may be the dominating side effects.

During processing of rapeseed, intact glucosinolates in the seeds may be hydrolyzed by the enzyme myrosinase, which is normally present in the seeds in a separate compartment. This generates a variety of products, some of which have goitrogenic effects (21). One of these products is inorganic thiocyanate (SCN⁻), which is a potent inhibitor of thyroid follicular cell iodine accumulation (22) by competitive inhibition of NIS (16). In higher concentrations thiocyanate also inhibits thyroid hormone synthesis by interfering with thyroid peroxidase (TPO).

**Rapeseed Feeding and Iodine Content of Cow’s Milk**

After conflicting reports on the degree and source of goitrogenicity of milk from cows fed diets containing glucosinolates, Papas et al. (23) performed a systematic study of the effects of feeding rapeseed meal to dairy cows. Three groups of cows were fed grain mixtures with soybean meal or one of two brands of rapeseed meal. Rapeseed feeding was accompanied by a substantial decrease in milk iodine content (Fig. 2). Urinary iodine excretions were not significantly altered in this study. Average thiocyanate intake was calculated to 0.2 mmol/d during soybean feeding and 21.3 mmol/d during rapeseed feeding. The milk thiocyanate concentrations were highest during rapeseed feeding but in general little thiocyanate was excreted in milk.

Similar findings have been reported by Hermansen et al. (24). They studied various aspects of rapeseed feeding and milk quality of dairy cows. Figure 3 shows results of an experiment where two levels of high glucosinolate rapeseed meal were used for feeding. The taste of milk was not affected, thiocyanate content was increased (but at low level), and notably, milk iodine content was reduced to 17% of control by the high-level rapeseed feeding. In this study, several other experiments substantiated the inhibitory effect of rapeseed on milk iodine content and that this correlated to the thiocyanate intake.

Many studies of domestic animals have demonstrated similar findings during rapeseed feeding both with high and low iodine intake. Many studies of domestic animals have demonstrated similar findings during rapeseed feeding both with high and low iodine intake.

**FIG. 3.** Taste of milk and content of thiocyanate and iodine during feeding with high glucosinolate rapeseed meal. Eighteen high-yielding cows were randomly assigned to control (without rapeseed) and two levels of rapeseed intake for 3 weeks. Taste scores of whole milk immediately and after 5 days of storage were not different. Thiocyanate in milk was significantly higher and iodine significantly lower during rapeseed feeding ($p < 0.001$). Values are per cent of control taste score without storage. Data from Hermansen et al. (24).

**FIG. 4.** Effect of rapeseed meal feeding with or without iodine supplements on mean serum thyroxine ($T_4$) in sows and their piglets. Sixteen pregnant German Landrace sows received standard diet with iodine supplements 150 μg/kg diet during gestation. During lactation groups of four sows received soybean meal (control) with or without iodine supplements 100 μg/kg diet or rapeseed meal with or without iodine. Venous blood samples from sows and two piglets per litter were taken at day 23 of lactation. Serum $T_4$ was significantly lower in piglets of sows receiving rapeseed without iodine supplements ($p < 0.05$). Data from Schöne et al. (29).
low glucosinolate variants. The largest series has been conducted by Schöne and collaborators from The Agricultural Institute of Thuringia in Jena, Germany (20,25,27–29). A few of their results will be presented.

**Rapeseed Feeding of Sows and Thyroid Function of Piglets**

Germany has for many years been a low-iodine intake area. In East Germany, pig diets containing high-glucosinolate rapeseed meal were used without supplementary iodine until 1986. This led to myxedema of the pigs, and a high frequency of stillborn piglets with various abnormalities (25), much like the piglet disease described in certain parts of the United States in the early part of the 20th century, before farmers started to iodine-supplement their pigs (26) (iodine supplementation to humans in these districts came later).

Series of experiments on intake of rapeseed (or purified glucosinolates) in pigs in Jena have shown that rapeseed feeding may induce goitre with a low iodine content of the thyroid and with a fall in serum thyroxine (T₄) whereas serum triiodothyronine (T₃) is relatively better preserved. During rapeseed feeding serum and urine levels of thiocyanate become high, whereas only small amounts of thiocyanate are excreted in milk. At low to medium levels of intake, all effects on the thyroid can be prevented by iodine supplementation, but not at high levels of intake (20,25,27–29).

The pattern is compatible with the inhibitory effects of thiocyanate on thyroid iodine uptake and organification. However, rapeseed contains other inhibitors of TPO that

![Graph](image-url)

**FIG. 5.** Mean serum thiocyanate (SCN⁻) in sows and their piglets after feeding the sows with soybean or rapeseed meal for 23 days of lactation. The same experiment as shown in Figure 4. Serum thiocyanate was significantly higher during rapeseed feeding in both sows and piglets (p < 0.05). Data from Schöne et al. (29).

![Graph](image-url)

**FIG. 6.** Mean iodine concentration of sow milk at the 23rd day of lactation. Groups of four sows were fed soybean or rapeseed without iodine supplements or with iodine 0.1 mg or 1 mg/kg diet. Data from Schöne et al. (29).
may participate in development of hypothyroidism at high glucosinolate intake levels (21).

Of particular interest are studies investigating the effect of rapeseed feeding of sows on thyroid function and iodine status of piglets (25,29). Figure 4 shows the results of randomly assigning pregnant pigs just before farrowing to diets based on soybean or rapeseed with or without iodine supplements. At the doses of protein-rich feed and iodine supplement used, serum T4 was not different in the groups of sows at day 23 of lactation. However, piglets of sows receiving rapeseed without iodine supplementation showed a considerable decrease in serum T4. This pattern was probably not a result of direct thiocyanate effect on the piglet thyroid. The sows had an eightfold increase in serum thiocyanate when they received rapeseed, but this was much less in the piglets (Fig. 5), and the sows’ milk contained little thiocyanate (data not shown). Several experiments in the study showed that the impaired thyroid function of the piglets correlated to a low iodine content of the sows’ milk during rapeseed feeding. Figure 6 shows the effect of different levels of iodine supplementation in combination with soybean or rapeseed. Milk iodine content increased drastically with the iodine intake during soybean feeding, but only moderately during rapeseed feeding. In this study also colostrum iodine content was much decreased by rapeseed (15 ± 4 μg/mL vs. soybean control 86 ± 27 μg/L, n = 4, mean ± standard deviation [SD], p < 0.001).

The various studies indicate that thiocyanate generated from glucosinolates in rapeseed inhibits NIS in the mammary gland of the lactating animal. This leads to a low iodine content of milk, and thereby an impaired thyroid function in the piglet, because of iodine deficiency.

Intake of Thiocyanate Generating Food and Development of Myxedematous Cretinism

The effect of thiocyanate in feeding on iodine content of milk in the lactating cow and sow has some implications for our understanding of iodine deficiency in breastfed children. If the area where the mother and child are living is characterized by iodine deficiency and the diet of the mother is rich in thiocyanate or substances generating thiocyanate, the iodine content of mothers’ milk will be low (30). Hence, the child may be severely thyroid hormone deficient because of lack of iodine, even if the thiocyanate excretion in milk is low.

In areas of the Congo where inhabitants had severe iodine deficiency and a high ingestion of cassava with a high serum SCN−, a high prevalence of cretinism was found (31,32). This was predominantly myxedematous cretinism, which is presumably caused by dominance of iodine deficiency in late fetal life and during the first years (33). Neurologic cretinism, on the other hand, may be founded approximately midgestation, where thyroid hormones of maternal origin are still of main importance for fetal brain development (34).

Thiocyanate may impair iodine nutrition in the breastfed child by inhibition of iodine transport into milk. Possibly, thiocyanate may also inhibit NIS in the placenta and thereby impair iodine deficiency mediated upregulation of placental iodine transport as well as upregulation of NIS in the fetal thyroid (35,36). Such transport supplies iodine to fetal thyroid hormone synthesis, which is the main source of thyroid hormone to the fetus in late gestation (34). Hence, the combination of iodine deficiency and high thiocyanate intake by the pregnant and lactating woman may more severely affect fetal and neonatal thyroid gland function, whereas iodine deficiency alone may give relatively more weight to fetal brain damage caused by insufficient maternal thyroid function.

Conclusion

In many populations iodine in dairy products constitutes a considerable part of iodine intake. The content of iodine in milk seems to vary with the iodine content of diet, but may be influenced by substances inhibiting NIS. Still another factor of importance for the iodine concentration in consumer milk is the use of iodine disinfectants in farming and dairies. Surveillance of consumer milk iodine content is advisable. Unexpected alterations of milk iodine content may retrospectively be deemed of value (3), but this is an unpredictable and hazardous way of preventing thyroid diseases in the population.

References


Address reprint requests to:
Peter Laurberg
Department of Endocrinology and Medicine
Aalborg Hospital
DK-9000 Aalborg
Denmark

E-mail: Laurberg@as.nja.dk