

# The Placenta Is Capable of Compensating for Smoking-Induced Thiocyanate Inhibition of Its Iodide Symporter

# Albert G. Burger

Andersen SL, Nøhr SB, Wu CS, Olsen J, Pedersen KM, Laurberg P. Thyroglobulin in smoking mothers and their newborns at delivery suggests autoregulation of placental iodide transport overcoming thiocyanate inhibition. Eur J Endocrinol. February 26, 2013 [Epub ahead of print].

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### **Background**

Blood levels of thiocyanate are known to be increased in smokers. It has been reported that in a population exposed to moderate iodine deficiency hypothyroidism is more severe in smokers than in nonsmokers (1). Thiocyanate inhibits the sodium iodide symporter (NIS), which is the main thyroidal iodide transporter. NIS is also present in tissues other than the thyroid, such as the placenta and the lactating mammary gland. In the case of partial inhibition of NIS by thiocyanate, thyroid activity gradually increases in order to overcome the inhibition. This compensatory mechanism is reflected by increased serum thyroglobulin levels. The purpose of the article under discussion was to determine whether compensating mechanisms capable of overcoming NIS inhibition by thiocyanate also exist in the placental-fetal unit.

#### **Methods**

The study was performed before the introduction of mandatory iodine supplementation in Denmark (year 2000). A total of 140 healthy pregnant women were studied. All women were clinically judged to be free of any thyroid problems. Maternal-blood and cord-blood samples were obtained at delivery for the measurement of thyroglobulin. On day 5, breast milk and a fetal urine sample were obtained for the measurement of iodine. The history of smoking reported by the study subjects was verified by measuring a serum metabolite of nicotine. The correlation was excellent.

#### **Results**

Forty-seven of the 140 mothers were given an iodine supplement of 150 mg per day during the pregnancy. The number of smokers was similar in the group receiving iodine and those not receiving iodine, and urinary iodide concentrations were similar in smoking and nonsmoking mothers. In contrast, urinary iodine in breast-fed newborns from smoking mothers was significantly decreased. Moreover, breast milk iodine in smokers was only half of that in the controls.

As expected, there was a marked difference in serum thyroglobulin depending on iodine supplementation (maternal serum, 14 and 29 mg/L in the group on supplemental iodine and those not on supplemental iodine, respectively; cord serum, 13 vs. 60 mg/L). In addition, smoking increased maternal serum thyroglobulin independently of iodine supplementation by a factor of 1.56 and increased cord blood by a factor of 1.43. Not surprisingly, the effect was more striking in mothers without iodine supplementation. Since thiocyanate inhibits NIS, it was interesting to compare cord-blood to maternal-blood thyroglobulin levels in smokers and nonsmokers, with and without iodine supplementation. Unexpectedly, the ratio was not affected by smoking or by iodine supplementation.

#### **Conclusions**

In an area of moderate iodine deficiency, smoking, with its consequence of increased serum thiocyanate levels is associated with increased maternal-continued on next page



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and cord-blood thyroglobulin levels. In mothers on moderate iodine supplementation, the thyroglobulin levels are lower than in mothers not receiving iodine supplementation, but the difference between smokers and nonsmokers is still present. However, the ratio of serum thyroglobulin in a given mother and her child was not altered by smoking or by iodine supplementation.

#### **ANALYSIS AND COMMENTARY** • •

It is well known that thiocyanate inhibits NIS and that thyroidal autoregulation of its activity is able to compensate for this interference. In contrast, although the maternal breast also expresses NIS, there appears to be no autoregulation in this tissue, since the iodine content of maternal milk is decreased by increased thiocyanate serum levels. The placental iodide transport is closer to that of the thyroid: indeed, it is assumed that it is regulated, at least to some extent, by human chorionic gonadotropin (HCG) stimulation. In addition to NIS, the placenta possesses other transporters of iodide that are not blocked by thiocyanate. Yet there is still a lot of uncertainty in this field. In the present article, the authors show that despite smoking and moderate iodine deficiency the ratio between the maternal and fetal thyroglobulin levels is not altered. This finding is taken to indicate that the placenta can also adjust to the partial inhibition of NIS by thiocyanate.

In clinical medicine it is often difficult to prove a concept. The authors believe that placental autoregulation is evidenced by the absence of a change in thyroglobulin ratio between mother and child when there is exposure to thiocyanate. Yet other explanations cannot be excluded; for instance, under the influence of thiocyanate, maternal iodide concentrations could increase, compensating for the decreased iodide uptake by the placenta.

Since smoking during pregnancy is widely discouraged, it is likely that the prevalence of smoking by child-bearing women has greatly decreased. There are many reasons for this recommendation, such as the fact that other aspects of endocrine function are perturbed by smoking (2). In this respect it is interesting to note the finding by these authors that infants breast-fed by smoking mothers have a markedly decreased urinary iodine excretion, requiring a compensatory increase in thyroid function.

#### References

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- 2. Kapoor D, Jones TH. Smoking and hormones in health and endocrine disorders. Eur J Endocrinol 2005;152:491-9.