

## Reply

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Dear Editor,

We read with interest the comments and suggestions of Dinc et al. [1] regarding our paper [2].

The authors state that an iodine supplementation of 150 µg/day was not adequate in women included in our study. However, this dosage is the recommendation of experts from the ATA (150 µg/day supplementation [3]) and the Endocrine Society (150–200 µg/day [4]). Thus, the dosage we used in our study should be adequate. In addition, the initial urinary iodine excretion (UIE) of >100 µg/l (which reflects at equilibrium an average daily intake >150 µg/day [5]) plus the 150-µg supplementation corresponding to a daily intake of around 300 µg is clearly above the minimum recommended 250 µg/day. Furthermore, UIE in our population showed that iodine deficiency was usually mild at the beginning; in the supplemented group in the third trimester, the median UIE reached 160 µg/l, suggesting iodine sufficiency. As in all studies, there is a wide range of values showing that some women remain with UIE below the theoretical 150-µg threshold. However, if UIE is the current reference tool for assessing iodine deficiency at the population level, it is not valid at the individual level, as it does not reflect a steady iodine status for a given woman [5].

Regarding the comment on kidney failure, this was not an issue in our population of healthy pregnant women.

Regarding the timing of supplementation, in France there is no recommendation for systematic iodine supplementation in all women planning a pregnancy. Our study targeted normal women seen in early pregnancy in a clinical setting, thus we had no access to women before pregnancy. A prospective randomized interventional study on supplementation before pregnancy was not feasible for us.

Regarding smoking, which seems the main interest of Dinc et al. [1], we have the following comments. UIE in the first trimester was already lower in smokers; however, the numbers are small. We know well the interesting epidemiological paper by Vanderver et al. [6] reporting data of the NHANES mostly outside pregnancy. However, this is a very different study whose design does not really allow comparison with our study. The populations studied are different: US versus European (different policies of iodine prophylaxis), mostly outside pregnancy versus pregnant, unselected versus selected normal women in our case, etc. The effect of tobacco on thyroid function is very complex with some conflicting data. The NHANES concluded that iodine supplementation should be considered cautiously in US pregnant smokers, but mainly when UIE was >200 µg/l and particularly in cases of iodine excess. They stated that this was a 'new approach that needed further investigation'. Additional

studies targeting maternal smoking are welcome.

Regarding anti-Tg antibodies, 7 patients (4 smokers, 3 nonsmokers) were initially positive (in the first trimester), but mostly just above the threshold of positivity, except for 2 patients >100 IU/ml (1 smoker, 1 nonsmoker). Six (3 smokers and 3 nonsmokers) out of 7 became negative by the time of delivery, as autoimmunity classically decreases throughout pregnancy. Thus, in our series, limited in numbers, smoking is not associated with decreased anti-Tg antibodies. Of note, none of our patients had positive anti-TPO (exclusion criteria for our study). Thus, we cannot extrapolate the potential effect of smoking in women with both TPO and anti-Tg antibodies.

We feel that the last paragraph does not apply to the population studied, since we had selected normal women without TPO antibodies or a personal history of thyroid disease, etc. We agree with the authors that further studies are required to clarify the respective effect of maternal smoking and iodine supplementation on thyroid function in an unselected population.

### Disclosure Statement

The authors have no conflicts of interest to disclose.

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