



## HYPOTHYROIDISM

# High doses of soy phytoestrogen are a risk factor in the progression of subclinical to overt hypothyroidism

### BACKGROUND

Soy foods are an important part of the diets of Asian people and are becoming increasingly popular in many non-Asian countries, including the United States. Soy foods are rich in phytoestrogens, which are thought to have many beneficial effects on cardiovascular health. Measures of cardiovascular health possibly affected by phytoestrogens include blood pressure, insulin sensitivity and markers of inflammation. Phytoestrogens also are thought to have beneficial to bone health and are said to be protective also against breast and prostate cancer. Soy also has long been thought to interfere with absorption of thyroid hormone from the stomach. Because of this, there has been concern that soy may worsen thyroid function, particularly in people with pre-existing mild hypothyroidism (underactive thyroid). This study examined the effect of soy on thyroid function and markers of cardiovascular health in patients with mild hypothyroidism.

### THE FULL ARTICLE TITLE:

Sathyapalan, T, et al. The effect of soy phytoestrogen supplementation on thyroid status and cardiovascular risk markers in patients with subclinical hypothyroidism: a randomized, double-blind, crossover study, *J Clinical Endocrinol Metab* 2011; 96 (5): 1442-49

### SUMMARY OF THE STUDY

Sixty patients (age 44 to 70 years) with subclinical hypothyroidism (TSH between 5 and 15 mU/L and normal serum free thyroxine  $T_4$ ) participated in the study. Patients were randomly assigned to low-dose phytoestrogen (30 grams of soy protein with 2 mg of phytoestrogens, typical of a Western diet) or high-dose phytoestrogen (30 grams of soy protein with 16 mg of phytoestrogens, representative of a vegetarian diet) for 8 weeks and then the groups were reversed after 8 weeks on a normal diet. Patients were followed and evaluated for development of overt hypothyroidism (serum TSH >10 mU/L and a low free  $T_4$ ).

Six patients (10%) developed clinical hypothyroidism after high-dose phytoestrogen but none after low-dose phytoestrogen. These patients were started on levothyroxine and continued to receive this treatment after 6 months. All six patients were women and only one of them had positive TPO antibodies (a measure of autoimmune thyroid disease). Neither baseline thyroid function tests, nor thyroid antibody measurement were helpful to predict progression from subclinical to overt hypothyroidism in patients receiving high dose phytoestrogen supplementation.

After high dose phytoestrogen supplementation, there was an improvement in blood pressure and insulin sensitivity and a reduction in hsCRP (a marker of inflammation), all of which suggest improved cardiovascular health markers.

### WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This is the first study to show that dietary supplementation with very high doses of soy phytoestrogen (at levels typical of a vegetarian diet), may result in a 3-fold increase in the risk of progression from subclinical to overt hypothyroidism, suggesting that vegetarian patients with mild subclinical hypothyroidism may need more careful monitoring of thyroid function. The mechanism for this effect is not well understood. On the other hand, high dose phytoestrogen also resulted in improvement in cardiovascular risk factors despite worsening of thyroid function and may be beneficial to patients with increased cardiovascular risk.

— M. Regina Castro, MD

### ATA THYROID BROCHURE LINKS

Hypothyroidism: [http://thyroid.org/patients/patient\\_brochures/hypothyroidism.html](http://thyroid.org/patients/patient_brochures/hypothyroidism.html)

Thyroid Function Tests: [http://thyroid.org/patients/patient\\_brochures/function\\_tests.html](http://thyroid.org/patients/patient_brochures/function_tests.html)

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## **HYPOTHYROIDISM, continued**

### **ABBREVIATIONS & DEFINITIONS**

**Phytoestrogens:** a group of compounds naturally found in some plants that have structural similarity to estradiol (the main female sex-hormone), are also called “dietary estrogens and can have some estrogen-like effects.

**Hypothyroidism:** a condition where the thyroid gland is underactive and doesn't produce enough thyroid hormone. Treatment requires taking thyroid hormone pills.

**Subclinical Hypothyroidism:** a mild form of hypothyroidism where the only abnormal hormone level is an increased TSH. There is controversy as to whether this should be treated or not.

**Overt Hypothyroidism:** clear hypothyroidism an increased TSH and a decreased T<sub>4</sub> level. All patients

with overt hypothyroidism are usually treated with thyroid hormone pills.

**TPO antibodies:** these are antibodies that attack the thyroid instead of bacteria and viruses, they are a marker for autoimmune thyroid disease, which is the main underlying cause for hypothyroidism and hyperthyroidism in the United States.

**TSH: thyroid stimulating hormone** — produced by the pituitary gland that regulates thyroid function; also the best screening test to determine if the thyroid is functioning normally.

**Levothyroxine:** the major hormone produced by the thyroid gland and available in pill form as Levoxy<sup>TM</sup>, Synthroid<sup>TM</sup>, Levothroid<sup>TM</sup> and generic preparations.