

# The relative importance of genetic and environmental effects in the regulation of thyroid function and size

A study of healthy Danish twins

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## ABSTRACT

This PhD dissertation is based on collaboration between the Department of Endocrinology, Odense University Hospital, and The Danish Twin Registry, at the Institute of Public Health, Epidemiology, University of Southern Denmark.

Overt thyroid diseases such as autoimmune thyroid disease and goitre are common. These complex diseases develop on the basis of genetic susceptibility interacting with environmental triggers. The diagnosis is based on measurements such as thyroid function (i.e. thyrotropin (TSH), triiodothyronine (T3) and thyroxine (T4)) and thyroid size. The study of thyroid homeostasis in healthy individuals is crucial in trying to understand the pathways that eventually lead to thyroid disease.

The aims of the study were to: 1) to quantify the relative contributions of genetic and environmental effects on thyroid function and 2) quantify the relative contributions of genetic and environmental effects on thyroid size by a classical twin study.

A sample of healthy twin pairs was recruited from the Danish Twin Registry. Blood samples were drawn between 8 and 9 a.m., followed by a clinical examination including an ultrasonography of the thyroid gland. Serum TSH, free T4, and free T3 were determined.

At total of 756 twin pairs were examined. Due to missing blood samples, self-reported as well as biochemical thyroid disease, complete twin pairs were excluded; 1380 individuals (690 twin pairs) distributed in 284 monozygotic (MZ), 286 dizygotic (DZ) and 120 opposite sex (OS) twin pairs were included. A sub-sample including 520 individuals were investigated using ultrasound. Twin pairs with enlarged thyroid gland, were excluded.

Intraclass correlations were calculated adjusting for age, gender, and other covariates. Structural equation model fitting was performed using the programme Mx.

Intraclass correlations for serum TSH, free T4 and T3 concentrations as well as for thyroid volume were consistently higher for MZ than for DZ twin pairs. Adjusting for covariates, 64% (95% CI 57-70%) of the variation in serum TSH concentration was due to additive genetic effects, while unique environmental effects explained the remaining 0.36 (95% CI 31-43%). Genetic effects explained 65% (95% CI 58-71%) and 64% (95% CI 57-70%) of the variance for serum free T4 and free T3 concentrations, respectively.

For thyroid volume, 71% (95% CI 61-78%) of the total variance

was explained by genetic factors. In general, the covariates were only responsible for a minor part of the variation.

Genetic factors are of major aetiological importance for thyroid function and thyroid size in euthyroid, healthy individuals. The studies in this thesis may serve as a basis for future aetiological studies.