Maternal Thyroid Autoimmunity During Pregnancy and the Risk of Attention Deficit/Hyperactivity Problems in Children: The Generation R Study

Akhgar Ghassabian,1,2 Jacoba J. Bongers-Schokking,3 Yolanda B. de Rijke,4,5 Nina van Mil,1,2 Vincent W.V. Jaddoe,6,7 Sabine M.P.F. de Muinck Keizer-Schrama,3 Herbert Hooijkaas,8 Albert Hofman,6 Willy Visser,9 Gustavo C. Roman,10 Theo J. Visser,4 Frank C. Verhulst,2 and Henning Tiemeier2,6.

1The Generation R Study Group, Erasmus University Medical Center, Rotterdam, The Netherlands.
2Department of Child and Adolescent Psychiatry/Psychology, Erasmus University Medical Center-Sophia Children’s Hospital, Rotterdam, The Netherlands.
3Department of Endocrinology, Erasmus University Medical Center-Sophia Children’s Hospital, Rotterdam, The Netherlands.
4Department of Internal Medicine, Erasmus University Medical Center, Rotterdam, The Netherlands.
5Department of Clinical Chemistry, Erasmus University Medical Center-Sophia Children's Hospital, Rotterdam, The Netherlands.
6Department of Epidemiology, Erasmus University Medical Center, Rotterdam, The Netherlands.
7Department of Pediatrics, Erasmus University Medical Center-Sophia Children's Hospital, Rotterdam, The Netherlands.
8Department of Immunology, Erasmus University Medical Center, Rotterdam, The Netherlands.
9Department of Obstetrics and Gynecology, Erasmus University Medical Center-Sophia Children's Hospital, Rotterdam, The Netherlands.
10Department of Neurology, Methodist Neurological Institute, Houston, Texas

Thyroid. February 2012, 22(2): 178-186.

Background: Maternal thyroid status and autoimmunity during pregnancy have been associated with impaired development of the offspring in animal and human studies. Our objective was to examine whether elevated titers of maternal thyroid peroxidase antibodies (TPOAbs) in early pregnancy increased the risk of cognitive impairment and problem behavior in preschool children. Second, we aimed at exploring to what extent any effect on child behavior was mediated by maternal thyroid parameters during pregnancy.

Methods: In the Generation R Study, a population-based cohort of 3139 children and their mothers, we measured maternal thyroid parameters (thyrotropin [TSH], free Thyroxine, and TPOAbs) at 13.5±1.8 weeks of gestation. Children's verbal and nonverbal cognitive functioning was measured at 2.5 years using the Language Development Survey and the Parent Report of Children Abilities. At 3 years, children's behaviour was assessed using the Child Behavior Checklist.

Results: Elevated titers of TPOAbs during pregnancy did not predict the verbal and nonverbal cognitive functioning of the children. However, elevated titers of TPOAbs in mothers were associated with externalizing problems in children (odds ratio [OR]=1.64, 95% confidence
interval [CI]: 1.17-2.29, p=0.004). In particular, children of TPOAb positive mothers were at a higher risk of attention deficit/hyperactivity problems (OR=1.77, 95% CI: 1.15-2.72, p=0.01).

To explore whether the effect of maternal TPOAbs on child problem behavior was mediated by maternal thyroid parameters, we added maternal TSH to the model. After correcting for TSH, the effect of TPOAbs on externalising problems was attenuated slightly but remained significant (OR=1.56, 95% CI: 1.14, 2.14, p=0.005).

Conclusions: Our findings imply that the elevated titers of TPOAbs during pregnancy impact children's risk of problem behavior, in particular, attention deficit/hyperactivity. The observed effect is only partially explained by maternal TSH levels. These findings may point to a specific mechanism of Attention Deficit/Hyperactivity Disorder in children. Nevertheless, we can only speculate about public health implication of the study, as there is no specific treatment for TPOAb-positive pregnant women with normal thyroid function. Further investigation is needed to explore whether TPOAb-positive pregnant women and their children can benefit from close monitoring and early detection of developmental delay in populations at risk.

Address correspondence to: Henning Tiemeier, M.D., Ph.D.
E-mail: h.tiemeier@erasmusmc.nl