Maternal Thyroid Deficiency during Pregnancy and Neuropsychological Development of the Child

From 1987 to the late 1990s, James Haddow and his team of researchers at the Foundation for Blood Research in Scarborough, Maine, studied children born to women who had thyroid deficiencies while pregnant with those children. Haddow´s team focused on newborns who had normal thyroid function at the time of neonatal screening. They tested the intelligence quotient, or IQ, of the children, ages eight to eleven years, and found that all of the children born to thyroid-hormone deficient mothers performed less well than the control group. Haddow and his colleagues published the experiment and results, "Maternal Thyroid Deficiency during Pregnancy and Subsequent Neuropsychological Development of the Child," in 1999. Haddow and his team proposed that undetected low thyroid hormone production in mothers, or maternal hypothyroidism, could adversely affect the neuropsychological development of children.

Prior studies had supported the claim that before the twelfth week of human pregnancy, when the fetal thyroid gland becomes active, the pregnant mother is the sole source of thyroid hormones for the developing fetus. Therefore, if doctors were to prevent fetuses from developing defects by treating pregnant women whose thyroids produced lower than normal amounts of hormones, then those doctors had to intervene at specific times during normal development. This theory that the treatment of thyroid function is time sensitive convinced some to argue for screening programs for thyroid deficiency in pregnant women as early as their first doctor´s visit after becoming pregnant.

For nearly a century, researchers had associated hypothyroidism in women caused by iodine deficiencies during pregnancy with impaired mental development of those women's offspring. Researchers had identified iodine deficiency as a cause for thyroid deficiency in pregnant women and in fetuses, but they couldn't tell if the impaired mental development of the children resulted from maternal and fetal hypothyroidism, or maternal hypothyroidism alone. Regardless of cause, in the 1970s, health care officials implemented mass-screening programs for neonatal hypothyroidism around the world to diagnose and treat congenital hypothyroidism in neonates. These screening programs improved the outcomes for many children who were born with thyroid deficiencies, because those children received treatment for their time-sensitive condition within the first three months of birth. Beyond this three-month window, babies face irreversible impairment to their neuropsychological development.

Haddow and his team sought to determine whether or not maternal hypothyroidism alone was capable of affecting the neuropsychological development of developing fetuses and children. Haddow´s team identified women with thyroid deficiency during pregnancy, but whose newborns had thyroids that functioned normally at birth. The experimental design enabled them to attribute any adverse findings in the neuropsychological development of children to maternal thyroid deficiency, as opposed to fetal thyroid deficiency.

Researchers identified the women by obtaining serum samples collected from 25,216 pregnant women in Maine between January 1987 and March 1990. The samples were originally taken due to a statewide screening program for Down syndrome and open neural-tube defects, which was administered by the Foundation for Blood Research during women's second trimester. Haddow's team spent three years measuring the concentrations of thyrotropin and free thyroxine present in the blood samples using radioimmunoassay techniques. They found sixty-two women who were thyroid hormone deficient during pregnancy and who were willing to participate in Haddow´s study. The thyrotropin concentrations during their pregnancies determined thyroid deficiency. Fourteen of the sixty-two women reported that they had received treatment for hypothyroidism, but based on the

high thyrotropin concentrations in their blood samples, they hadn't received adequate treatment. Forty-seven of the women had concentration levels at or below the 99.7th percentile, representing very high concentrations of thyrotropin and consequently low thyroid gland function. Fifteen women represented milder cases of hypothyroidism, with thyrotopin concentrations between the 98th and 99.6th percentiles, representing low thyroid gland function but at lower serum thyrotropin concentration than did the other forty-seven women.

The researchers matched each woman recruited for the study, called a test subject, with two similar pregnant women, who served as controls and enabled researchers to compare results. These control subjects were selected according to five criteria with regard to the test subject and the offspring. First, the control subject was within one year of the test subject´s age at delivery. Second, the control subject had nearly the same number of years of education as the test subject. Third, the fetus of the control subject had to be within one week of the same gestational age as the fetus of the test subject at the time when the test subject was sampled. Fourth, the serum sample tested could be stored no longer than one month. Fifth, the control subject had to have a fetus of the same sex as the test subject's child.

Other factors influence the intellectual development of children, which Haddow's team considered for their results to be significant. To account for these factors, the researchers collected information about socioeconomic status, the presence, or absence of fathers or partners, and the education and employment of guardians. The team analyzed that data with statistical techniques that helps characterize and position individuals within a society. They found no significant socioeconomical differences found between the women with hypothyroidism and the women in the control group. After matching their mothers with control subjects, researchers tested the children's intelligence, attention spans, language and reading abilities, and school performance.

To measure intelligence of each child, researchers used the third edition of the Wechsler Intelligence Scale for Children (WISC), an intelligence test used to quantify the Intelligence Quotient (IQ) of an individual through paper tests. Proctors who were unaware of each child's status administered the tests. The results of the tests indicated that children affected by maternal hypothyroidism performed less well compared to unaffected children. Of those children affected by maternal hypothyroidism, those whose mothers did not receive treatment for hypothyroidism during their pregnancies received the lowest scores.

The average full-scale IQ score for the children of thyroid deficient mothers was seven points lower than the children in a control group, with nineteen percent of the affected children having IQ scores of eighty-five or lower, in contrast to five percent of the control children who had such scores. The WISC scoring index classifies scores of 115 to 85 within average range, and below eighty-five is classified as below average.

Haddow and his colleagues concluded that maternal hypothyroidism alone could adversely affect the neuropsychological development of the child. Due to this finding, they encouraged screening for hypothyroidism in all pregnant women. Haddow reasoned that as a pregnant woman is the sole source of thyroid hormones for a fetus until the fetus's thyroid gland becomes active at twelve weeks gestation, doctors should screen for and treat thyroid deficiencies in pregnant women within the first trimester of pregnancy.

Since they published their results in 1999, Haddow and his team´s report has been cited greater than 1,300 times. Before the team's research, doctors often advised pregnant women to discontinue the use of thyroid medication, in fear that thyroid medication might harm the fetus. In 2007, the American Congress of Obstetricians and Gynecologists in the US recommended that only women classified as high-risk should receive screening for thyroid disease while pregnant, unless otherwise decided by the patient and her physician. High-risk women are those with personal or family histories of thyroid disease, autoimmune disorders, goiters, diabetes, or with histories of preterm deliveries or miscarriages. In 2008, the US Preventive Services Task Force recommended that all newborns be tested for hypothyroidism.

Sources

1. American Congress of Obstetricians and Gynecologists. ”Subclinical Hypothyroidism in Pregnancy.” October, 2007. http://www.acog.org/Resources_And_Publications/Committee_Opinions/Committee_on_Obstetric_Practice/Subclinical_Hypothyroidism_in_Pregnancy (Accessed April 20, 2012).
2. American Thyroid Association. ”Thyroid Disease and Pregnancy.” June 4, 2012. http://www.thyroid.org/thyroid-disease-and-pregnancy/ (Accessed July 9, 2014).
3. Cooper, Shawn. The Clinical Use and Interpretation of Wechsler Intelligence Scale for Children, Third Edition. Springfield, IL : Charles C. Thomas, 1995.
4. Dussalt, Jean H., and Delbert A. Fisher. ”Thyroid Function in Mothers of Hypothyroid Newborns.” Obstetrics and Gynecology 93 (1999): 15–20. http://journals.lww.com/greenjournal/Fulltext/1999/01000/Thyroid_Function_in_Mothers_of_Hypothyroid.4.aspx (Accessed July 9, 2014).
5. Glinoer, Daniel. ”Systematic Screening and Management of Hypothyroidism and Hyperthyroidism during Pregnancy.” Technology, Education, Management, Informatics Journal 9 (1998): 403–11.
6. Haddow, James E., Glenn E. Palomaki, Walter C. Allan, Josephine R. Williams, George J. Knight, June Gagnon, Cheryl E. O´Heir, Marvin L. Mitchell, Rosalie J. Hermos, Susan E. Waisbren, James D. Faix, and Robert Z. Klein. ”Maternal Thyroid Deficiency During Pregnancy and Subsequent Neuropsychological Development of the Child.” The New England Journal of Medicine 341 (1999): 549–55. http://www.nejm.org/doi/full/10.1056/NEJM199908193410801#t=articleTop (Accessed July 9, 2014).
7. Harris, Russel P., Mark Helfand, Steven H. Woolf, Kathleen N. Lohr, Cynthia D. Mulrow, Steven M. Teutsch, David Atkins. ”Current Methods of the US Preventive Services Task Force: a Review of the Process.” American Journal of Preventative Medicine 20 (2001): 21–35. http://archive.ahrq.gov/clinic/ajpmsuppl/review.pdf (Accessed July 9, 2014).
8. Gharib, Hossein, Rhoda H. Cobin, and Richard A. Dickey. ”Subclinical Hypothyroidism during Pregnancy: Position Statement from the American Association of Clinical Endocrinologists.” Endocrine Practice 5 (1999): 367–8.
9. Gharib, Hossein, R. Michael Tuttle, H. Jack Baskin, Lisa H. Fish, Peter A. Singer, and Michael T. McDermott. ”Subclinical thyroid dysfunction: a joint statement on management from the American Association of Clinical Endocrinologists, the American Thyroid Association, and the Endocrine Society.” The Journal of Clinical Endocrinology and Metabolism 90 (2005): 581–585. http://press.endocrine.org/doi/full/10.1210/jc.2004-1231 (Accessed July 9, 2014).
10. Mestmen, Jorge. ”Diagnosis and Management of Maternal and Fetal Thyroid Disorders.” Current Opinion in Gynecology and Obstetrics 11 (1999): 167–75.
11. U.S. Preventive Services Task Force. ”Screening for Congenital Hypothyroidism (CH).” March, 2008. http://www.uspreventiveservicestaskforce.org/uspstf/uspscghy.htm (Accessed July 9, 2014).