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The relationships between blood lead levels and serum thyroid stimulating hormone and total thyroxine in the third National Health and Nutrition Examination Survey

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Abstract

Regression analysis was used to estimate and test for relationships between the blood lead concentration and the concentrations of serum thyroid stimulating hormone and serum total thyroxine in adults, 20 years and older, participating in the third National Health and Nutrition Examination Survey. No relationship was found between the blood lead level and the concentration of serum thyroid stimulating hormone. The serum total thyroxine concentration decreased as the blood lead level increased in women, but not in men. The lowest concentration of blood lead at which a relationship could be detected was 2.1 μg/dL and 3.9 μg/dL for the non-pregnant and pregnant women, respectively. Hypothetical mechanisms of the action of lead are discussed.

Keywords

Blood lead; Thyroid stimulating hormone; Thyroxine; NHANES III

1. Introduction

Cross-sectional studies of the effects of occupational exposures to lead on thyroid hormone concentrations in the blood have produced inconsistent results. For example, Robins, Cullen, Connors, and Kayne [1] found an inverse relationship between free thyroxine and blood lead concentrations in 47 men who worked on the shop floor of a brass foundry. The average whole blood lead levels of the men ranged from 16 to 127 μg/dL. Refowitz [2] reported no relationships between the total thyroxine or free thyroxine concentrations and the whole blood lead concentration in 58 men working at a secondary copper smelter. The whole blood

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Human subjects review

No human subjects review was required.

Conflict of interest

None.

lead levels of the men ranged from 5 to 60 μg/dL. A recent meta-analysis of occupational studies [3] found no effect of lead exposure on thyroid hormone concentrations. The workers in the studies were predominantly men, so the lack of relationship does not necessarily indicate the lack of an effect in women.

Environmental studies have found relationships with blood lead in women and men. Abdelouahab et al. [4] studied a group of 124 men and 87 women who lived in lakeside communities and ate freshwater fish. They found an inverse relationship between the serum concentration of thyroid stimulating hormone and the whole blood lead concentration in the women, but not in the men. They found a direct relationship between the concentrations of total triiodothyronine and blood lead in women, but not in men. The blood concentration of total thyroxine was not related to the blood lead concentration in women or men. The median blood lead concentration of the women was 1.74 μg/dL and of the men was 3.10 μg/dL. Meeker et al. [5] found that the serum concentration of thyroid stimulating hormone decreased as the whole blood lead concentration increased in 219 men participating in a study of environmental influences on male reproductive health. The median blood lead concentration of the men was 1.5 μg/dL.

The thyroid hormone data from the third National Health and Nutrition Examination Survey (NHANES III) has not been analyzed with respect to lead. The data provide an opportunity to test for sex-specific effects of lead on thyroid hormones in a large population. NHANES III was conducted between 1988 and 1994. The thyroid hormones measured were thyroid stimulating hormone and total thyroxine and the sample size for the thyroid hormones was 16,573. The results from the analysis of the NHANES III data are reported here. The average blood lead level of the persons used in the analysis was 3.55 μg/dL.

2. Material and methods

2.1. Subjects

The subjects in NHANES III were civilian, non-institutionalized persons in the United States 2 months of age or older. The survey was conducted from 1988 to 1994. Approximately 40,000 persons were selected to participate in the survey. The subjects for the present study were 16,573 men and women, 20 years old or older, who participated in an examination at a mobile examination center.

Subjects attended one of three daily sessions at a mobile examination center: morning, afternoon, or evening. The sessions could last up to three and one-half hours. Subjects were asked to fast over-night for the morning session and for six hours before an afternoon or evening session.

2.2. Sampling

The sample design was a stratified, multistage probability design. In the first stage of sampling, 81 primary sampling units (PSUs) were selected. The PSUs were individual counties or adjacent counties. Thirteen of the large PSUs were divided into 21 survey locations and the remaining 68 PSUs had one survey location. The 89 survey locations or ‘stands’ were randomly divided into two phases. Phase I consisted of 44 locations visited

from 1988 to 1991. Phase II consisted of 45 locations visited from 1991 to 1994. Later stages of sampling included area segments, households, and sample persons. Details about the survey design can be found in Ezzati, Massey, Waksberg, Chu, and Maurer [6].

2.3. Blood lead

Venous blood samples were taken at mobile examination centers or during home examinations given to persons who could not go to a mobile examination center. Blood lead was measured by atomic absorption spectrometry in persons one year and older. The limit of detection for the blood lead measurements was 1 μg/dL. Values below the limit of detection were assigned a value of 0.7 μg/dL. The percent of measured values below the limit of detection was 7.93%.

Details about the measurement of blood lead and the other blood and urine measurements can be found in the NHANES III laboratory manual [7].

2.4. Serum thyroid hormones and antibodies

Thyroid stimulating hormone was measured in blood serum samples of persons 12 years and older by a chemiluminescence immunometric assay. The limit of detection was 0.01 μU/mL. Values below the limit of detection were assigned a value of 0.00 μU/mL. The percent of measured values below the limit of detection was 0.41%.

Total circulating thyroxine was measured in blood serum samples of persons 13 years and older by an enzyme-based homogenous immunoassay. The limit of detection was 0.5 μg/dL. Values below the limit of detection were assigned a value of 0.4 μg/dL. The percent of measured values below the limit of detection was 0.21%.

Serum antimicrosomal antibody was measured by radio-immunoassay in persons 12 years and older. The limit of detection was 0.5 U/mL. Values below the limit of detection were assigned a value of 0.3 U/mL. The percent of measured values below the limit of detection was 86.75%.

Serum anti-thyroglobulin antibody was measured by radio-immunoassay in persons 12 years and older. The limit of detection was 1.0 U/mL. Values below the limit of detection were assigned a value of 0.7 U/mL. The percent of measured values below the limit of detection was 89.22%.

2.5. Urinary creatinine and iodine

Spot urine specimens were collected at mobile examination centers by the clean-catch technique into sterile 250 mL polyethylene containers.

A Jaffé rate reaction, where creatinine reacts with picrate in an alkaline solution to form a red creatinine-picrate complex, was used to measure urinary creatinine in persons six years or older. The limit of detection was 10 mg/dL. Values below the limit of detection were assigned a value of 7.9 mg/dL. The percent of measured values below the limit of detection was 0.37%.

Urinary iodine is measured by using the reduction-oxidation reaction between ceric and arsenite catalyzed by iodide in persons six years or older. The limit of detection was 0.2 μg/dL. Values below the limit of detection were assigned a value of 0.1 μg/dL. The percent of measured values below the limit of detection was 0.03%.

2.6. Serum cotinine

Cotinine was measured in blood serum samples of persons four years and older by an enzyme immunoassay. The limit of detection was 0.05 ng/mL. Values below the limit of detection were assigned a value of 0.035 ng/mL. The percent of measured values below the limit of detection was 12.15%.

2.7. Bone densitometry

The bone densities of five areas of the proximal femur were measured using dual energy x-ray absorptiometry. Measurements were made on women who were not pregnant and men, 20 years or older. The femoral neck, trochanter, intertrochanter, Ward's Triangle, and the total region were measured. Bone mineral density of the total region (g/cm^2) was used in the present analysis. The missing values for pregnant women were set to zero so that they would not be excluded from the analysis.

2.8. Demographic and questionnaire variables

The demographic variables that were used included race-ethnicity (DMARETHN), sex (HSSEX), and age at interview (HSAGEIR). Ages of 90 years old or above were coded as 90 years old.

A variable (MXPSESSR) indicating the period of day that a person was examined at a mobile examination center was used. Examinations were scheduled for morning, afternoon, and evening sessions.

Body mass index (BMPBMI) was calculated from the measurements of the weight in kilograms (BMPWT) and the standing height in centimeters (BMPHT).

The variable used to indicate pregnancy (MAPF12R) was from the Mobile Examination Center Adult Questionnaire that was administered to all persons, 17 years or older, that were examined at a mobile examination center. Positive responses were coded as '1'. 'Blank but applicable' and 'Don't know' were coded as missing. All other values were coded as '0'.

Two questions were used to determine menopausal status: 'Have you had a period in the past 12 months?' (MAPF21) and 'Were both ovaries removed or only one?' (MAPF28). From these variables, a variable called 'menopause' was created with three levels: no, yes (women who had not had a period in the last 12 months), and surgical (women with both ovaries removed). The levels of menopause are mutually exclusive.

One question was used to determine hormone pill use: 'How many months ago did you stop taking estrogen or female hormone pills or are you still taking them?' (MAPF39S), one question was used to determine hormone use via vaginal creams, suppositories, or injections: 'How many months ago did you stop using the vaginal cream, suppository, or injection or

are you still taking them?' (MAPF43S), and one question was used to determine hormone patch use: 'How many months ago did you stop using the hormone patches or are you still using them?' (MAPF47S).

A variable (PHPFAST) indicating the number of hours since a person last ate or drank was used. This variable was from the Phlebotomy Screening Questionnaire.

Two questions from the Household Adult Questionnaire were used to indicate thyroid disease: 'Has a doctor ever told you that you had goiter?' (HAC1J) and 'Has a doctor ever told you that you had other thyroid disease?' (HAC1K).

Variables (HAX9) which give the drug class codes of medications a person reports currently taking were used to determine thyroid or antithyroid drug use. From these variables, a variable called 'thyroid drug' was created with two levels: no and yes (a person reports currently taking one or more thyroid or antithyroid drugs).

2.9. Statistical analysis

The computer program SAS® (Release 9.4, SAS Institute, Inc., Cary, North Carolina) was used to analyze the survey data. Survey procedures were used that took into account the complex survey design. Two design variables were used, pseudo-PSU (SDPPSU6) and pseudo-stratum (SDPSTRA6). The total MEC-examined sample final weight (WTPFEX6) was used. Analytical guidelines for NHANES III are available [8,9].

Linear regression analysis was performed between the $\log_{10}$ serum thyroid stimulating hormone concentration and the $\log_{10}$ blood lead concentration. This model also included race-ethnicity, sex, age, session, body mass index, pregnant, menopause, hormone pill use, vaginal cream use, hormone patch use, urinary creatinine, $\log_{10}$ urinary iodine, $\log_{10}$ serum cotinine, serum thyroxine, $\log_{10}$ serum antimicrosomal antibody, $\log_{10}$ serum anti-thyroglobulin antibody, total bone mineral density, length of fast, goiter, other thyroid disease, and thyroid drug as covariates, as well as the sex × pregnant × $\log_{10}$ blood lead concentration interaction.

Linear regression analysis was also performed between serum thyroxine and the $\log_{10}$ blood lead concentration. This model also included race-ethnicity, sex, age, session, body mass index, pregnant, menopause, hormone pill use, vaginal cream use, hormone patch use, urinary creatinine, $\log_{10}$ urinary iodine, $\log_{10}$ serum cotinine, $\log_{10}$ serum antimicrosomal antibody, $\log_{10}$ serum anti-thyroglobulin antibody, total bone mineral density, length of fast, goiter, other thyroid disease, and thyroid drug as covariates, as well as the sex × pregnant × $\log_{10}$ blood lead concentration interaction.

In order to determine the lowest concentrations of blood lead at which a relationship could be detected, two variables for blood lead were created. If the lead value was less than or equal to a cutoff value, the first lead variable was assigned the value and the second lead variable was set to zero. If the lead value was greater than the cutoff value, the first lead variable was set to zero and the second lead variable was assigned the value. The cutoff value varied from the next to lowest value of blood lead to the highest value and was incremented in steps of 0.1. The slopes of the two lead variables were calculated at each

step. The lowest blood lead value at which a relationship could be detected was defined as the cutoff value for which the slope of the first lead variable was statistically significant ($p < 0.05$) at the cutoff value and all subsequent greater values. Covariates were included in the models, and separate estimates were made for each level of sex by including interaction terms with sex.

SigmaPlot® (Version 11.0, Systat Software, Inc., San Jose, California) was used to make the graph. Simple linear least squares regression was used to fit the data in the graphs.

3. Results

Table 1 shows estimates of the population means of the continuous variables. The minimum and maximum values in the table are statistics describing the sample and are not population estimates. Pregnant women were not included in the estimate of total bone mineral density. Table 2 shows population estimates of the mean concentrations of serum thyroid stimulating hormone and total thyroxine by classification variables.

Table 3 shows the estimated regression coefficients (slopes) for the continuous variables included in the linear regression models. The concentration of thyroid stimulating hormone was not statistically significantly related to the blood lead concentration. The concentration of total thyroxine statistically significantly decreased as the blood lead concentration increased.

Table 4 shows the estimated regression coefficients (slopes) for the sex × pregnant × $\log_{10}$ blood lead concentration interaction that was included in the linear regression models. For serum thyroid stimulating hormone, the interaction was not statistically significant, $F(2, 49) = 0.93$, $p = 0.4006$. None of the simple effects of blood lead were statistically significant. The slope for the pregnant females was not statistically significantly different from the slopes for the non-pregnant females ($p = 0.9481$) and males ($p = 0.7539$). The slope for the non-pregnant females was not statistically significantly different from the slope for the males ($p = 0.1798$). For serum total thyroxine, the interaction was statistically significant, $F(2, 49) = 7.02$, $p = 0.0021$. Serum total thyroxine decreased as the blood lead concentration increased in non-pregnant and pregnant females, but not in males. The slope for the pregnant females was statistically significantly less than the slopes for the non-pregnant females ($p = 0.0106$) and males ($p = 0.0013$). The slope for the non-pregnant females was not statistically significantly less than the slope for the males ($p = 0.0634$).

Fig. 1 shows the relationship between the serum thyroid stimulating hormone and blood lead concentrations by level of sex × pregnant. Fig. 2 shows the relationship between the serum total thyroxine and blood lead concentrations by level of sex × pregnant.

The lowest concentrations of blood lead at which a relationship could be detected are shown in Table 5. For serum total thyroxine, the lowest concentration was 2.1 μg/dL for the non-pregnant females and 3.9 μg/dL for the pregnant females.

4. Discussion

4.1. Thyroid stimulating hormone

No relationship was found between the blood lead level and the concentration of serum thyroid stimulating hormone in men or women.

In previous environmental studies, Abdelouahab et al. [4] found an inverse relationship between the concentrations of serum thyroid stimulating hormone and blood lead in women, but not in men, and Meeker et al. [5] found an inverse relationship in men. The median blood lead levels in these studies (1.74, 3.10, and 1.5 μg/dL) are similar to the mean blood lead level in the present study (3.55 μg/dL).

Abdelouahab et al. [4] included age, smoking status, selenium, total plasma lipid concentration, and oestro-progestative hormone intake as covariates for women. The men and women were analyzed in separate models. The age of the 87 women ranged from 18 to 70 years old. Concentrations of lead were log transformed. The concentrations of thyroid hormones were not.

Meeker et al. [5] included age, body mass index, and current smoking. The age of the 219 men ranged from 18 to 55 years old. Concentrations of lead were log transformed and grouped into quartiles. The concentrations of thyroid stimulating hormone were log transformed.

In the present analysis, removing all the covariates from the model for thyroid stimulating hormone did not result in statistically significant regression coefficients for blood lead for men ($b = 0.00730$, $p = 0.7132$), non-pregnant women ($b = 0.01899$, $p = 0.3186$), or pregnant women ($b = -0.02726$, $p = 0.8159$), so adjustment by the covariates was not responsible for the lack of statistical significance.

4.2. Thyroxine

The concentration of serum total thyroxine decreased as the blood lead level increased in non-pregnant and pregnant women, but not in men. The decrease was greatest in the pregnant women.

In a previous environmental study, Abdelouahab et al. [4] found no relationship between the concentrations of serum total thyroxine and blood lead in women or men. The regression coefficients for men ($b = -1.93$, $p > 0.10$) and women ($b = -0.36$, $p > 0.10$) were negative but not statistically significant. It is possible the sample size was not large enough to detect a relationship.

Two sex specific hypotheses can be made about the decreases in total thyroxine seen in the present study. First, lead could inhibit the sialylation of thyroid binding globulin by estrogens and reduce the concentration of thyroid binding globulin and thus total thyroxine in the blood. Thyroid binding globulin is a carrier protein that binds to thyroxine [10]. Estrogens increase the concentration of thyroid binding globulin and thyroxine [11]. Estrogens increase the amount of thyroid binding globulin that is sialylated [12]. Sialylated

thyroid biding globulin has a lower clearance rate in the liver than unsialylated thyroid binding globulin [13].

Secondly, during pregnancy lead could also inhibit the sialylation of human chorionic gonadotropin which would lead to a decrease in the production of thyroxine by the thyroid. Desialylated forms of human chorionic gonadotropin have a higher affinity for the thyroid stimulating hormone receptors in thyroid membranes [14]. A desialylated form of human chorionic gonadotropin has been shown to be an antagonist of adenylate cyclase activity induced by thyroid stimulating hormone [15].

4.3. Covariates

Covariates were chosen based on previous analyses of thyroid hormone data, especially, Hollowell et al. [16] and Blount et al. [17]. Urinary creatinine was included in the models to adjust for urine volume for urinary iodine. This method of adjustment is recommended by Barr et al. [18]. Serum total thyroxine was included as a covariate for serum thyroid stimulating hormone to control for an indirect effect of lead via the negative feedback of thyroxine [19].

Total bone mineral density was included as a covariate to control for the relationships between thyroid hormones and blood lead level due to effect of thyroid hormones on bone metabolisim. Thyroid hormones are necessary for bone growth and maintenance [20]. Thyroid stimulating hormone is positively related to bone mineral density in men [21] and women [22], and hyperthyroidism is associated with lower bone mineral density and a greater risk of fractures [23].

Lead is stored in bone [24] and can alter bone cell function [25], and blood lead levels are related to bone metabolism. In women 40 to 59 years old from NHANES III, there was an inverse relationship between blood lead level and bone mineral density [26]. Biological markers of bone turnover were positively related to blood lead levels in a study of Japanese female farmers [27].

4.4. Lowest concentration

The method for determining the lowest concentration was a modification of the method used by Lanphear, Dietrich, Auinger, and Cox [28]. They calculated regression coefficients between blood lead concentrations and cognitive performance in children with blood lead concentrations at < 10, < 7.5, < 5.0, and < 2.5 μg/dL, and determined the lowest subset in which the relationships were still statistically significant (< 5 μg/dL). Children were successively dropped out of the model at each step.

The modified method used here incremented the blood lead concentration by steps of 0.1 μg/dL to get a more precise estimate of the concentration at which the relationship becomes consistently statistically significant. Instead of dropping subjects out of the model, their blood lead levels are placed in a second blood lead variable so that the sample size remains constant.

For serum total thyroxine, the lowest concentration of blood lead at which a relationship could be detected was 2.1 μg/dL for the non-pregnant women and 3.9 μg/dL for the pregnant women. The current elevated blood lead level for adults as defined by the Centers for Disease Control and Prevention is ≥ 5 μg/dL (https://www.cdc.gov/niosh/topics/ables/default.html).

In terms of clinical significance, from Table 4, for the non-pregnant women a 10 times increase in blood lead, e.g., from 1 to 10 μg/dL, would result in a 0.5 μg/dL decrease in serum total thyroxine. For the pregnant women, a 10 times increase would result in a 2 μg/dL decrease in serum total thyroxine. The normal range for total thyroxine is 4.5 to 12.5 μg/dL (http://globalrph.com/labs/t/), so a 10 times increase would probably not be clinically relevant for a non-pregnant women. For a pregnant women, a 10 times increase could potentially take a woman below the normal range or into the normal range depending or what her initial level was.

5. Conclusion

Serum total thyroxine decreased as the blood lead concentration increased in women, but not in men. The decrease was greater in pregnant women. The lowest concentration of blood lead at which a relationship could be detected was 2.1 μg/dL and 3.9 μg/dL for the non-pregnant and pregnant women, respectively. Hypothetical mechanisms of the action of lead were discussed. If future occupational studies are done, they should include women.

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References

[1]. Robins JM, Cullen MR, Connors BB, Kayne RD, Depressed thyroid indexes associated with occupational exposure to inorganic lead, Arch. Intern. Med 143 (2) (1983) 220–224. [PubMed: 6600605]

[2]. Refowitz RM, Thyroid function and lead: no clear relationship, J. Occup. Med 26 (8) (1984) 579–583. [PubMed: 6481498]

[3]. Krieg EF Jr., A meta-analysis of studies investigating the effects of occupational lead exposure on thyroid hormones, Am. J. Ind. Med 59 (7) (2016) 583–590. [PubMed: 27094769]

[4]. Abdelouahab N, Mergler D, Takser L, Vanier C, St-Jean M, Baldwin M, Spear PA, Chan HM, Gender differences in the effects of organochlorines, mercury, and lead on thyroid hormone levels in lakeside communities of Quebec (Canada), Environ. Res 107 (3) (2008) 380–392. [PubMed: 18313043]

[5]. Meeker JD, Rossano MG, Protas B, Diamond MP, Puscheck E, Daly D, Paneth N, Wirth JJ, Multiple metals predict prolactin and thyrotropin (TSH) levels in men, Environ. Res 109 (7) (2009) 869–873. [PubMed: 19595304]

[6]. Ezzati TM, Massey JT, Waksberg J, Chu A, Maurer KR, Sample Design: Third National Health and Nutrition Examination Survey (DHHS Publication No. PHS 92–1387, Series 2, No. 113), National Center for Health Statistics, Hyattsville, Maryland, 1992.

[7]. Gunter EW, Lewis BG, Koncikowski SM, Laboratory Procedures Used for the Third National Health and Nutrition Evaluation Survey (NHANES III), 1988–1994, National Center for Health Statistics, Hyattsville, Maryland, 1996.

[8]. National center for health statistics, analytical and reporting guidelines, The Third National Health and Nutrition Examination Survey, NHANES III (1988–94), National Center for Health Statistics, Hyattsville, Maryland, 1996.

[9]. National center for health statistics, NHANES III Laboratory Data File Documentation (Catalog No. 76300), National Center for Health Statistics, Hyattsville, Maryland, 1996.

[10]. Refetoff S, De Groot LJ, Beck-Peccoz P, Chrousos G, Dungan K, Grossman A, Hershman JM, Koch C, McLachlan R, New M, Rebar R, Singer F, Vinik A, Weickert MO (Eds.), Thyroid Hormone Serum Transport Proteins: Structure, Properties, Genes and Transcriptional Regulation, Endotext, South Dartmouth (MA), 2000.

[11]. Arafah BM, Increased need for thyroxine in women with hypothyroidism during estrogen therapy, N. Engl. J. Med 344 (23) (2001) 1743–1749. [PubMed: 11396440]

[12]. Gärtner R, Henze R, Horn K, Pickardt CR, Scriba PC, Thyroxine-binding globulin: investigation of microheterogeneity, J. Clin. Endocrinol. Metab 52 (4) (1981) 657–664. [PubMed: 6782114]

[13]. Ain KB, Mori Y, Refetoff S, Reduced clearance rate of thyroxine-binding globulin (TBG) with increased sialylation: a mechanism for estrogen-induced elevation of serum TBG concentration, J. Clin. Endocrinol. Metab 65 (4) (1987) 689–696. [PubMed: 3116030]

[14]. Amir SM, Kasagi K, Ingbar SH, The role of subunit sialic acid in the thyrotropic and gonadotropic activities of human chorionic gonadotropin, Endocrinology 121 (1) (1987) 160–166. [PubMed: 3036467]

[15]. Carayon P, Amr S, Nisula B, A competitive antagonist of thyrotropin: asialo-choriogonadotropin, Biochem. Biophys. Res. Commun 97 (1) (1980) 69–74. [PubMed: 6257243]

[16]. Hollowell JG, Staehling NW, Flanders WD, Hannon WH, Gunter EW, Spencer CA, Braverman LE, Serum TSH, T_4, and thyroid antibodies in the United States population (1988 to 1994): National Health and Nutrition Examination Survey (NHANES III), J. Clin. Endocrinol. Metab 87 (2) (2002) 489–499. [PubMed: 11836274]

[17]. Blount BC, Pirkle JL, Osterloh JD, Valentin-Blasini L, Caldwell KL, Urinary perchlorate and thyroid hormone levels in adolescent and adult men and women living in the United States, Environ. Health Perspect 114 (12) (2006) 1865–1871. [PubMed: 17185277]

[18]. Barr DB, Wilder LC, Caudill SP, Gonzalez AJ, Needham LL, Pirkle JL, Urinary creatinine concentrations in the U.S. Population: implications for urinary biologic monitoring measurements, Environ. Health Perspect 113 (2) (2005) 192–200. [PubMed: 15687057]

[19]. Zoeller RT, Tan SW, Tyl RW, General background on the hypothalamic-pituitary-thyroid (HPT) axis, Crit. Rev. Toxicol 37 (1–2) (2007) 11–53. [PubMed: 17364704]

[20]. Bassett JHD, Williams GR, Role of thyroid hormones in skeletal development and bone maintenance, Endocr. Rev 37 (2) (2016) 135–187. [PubMed: 26862888]

[21]. Kim B-J, Lee SH, Bae SJ, Kim HK, Choe JW, Kim HY, Koh J-M, Kim GS, The association between serum thyrotropin (TSH) levels and bone mineral density in healthy euthyroid men, Clin. Endocrinol 73 (3) (2010) 396–403.

[22]. Morris MS, The association between serum thyroid-stimulating hormone in its reference range and bone status in postmenopausal American women, Bone 40 (4) (2007) 1128–1134. [PubMed: 17236836]

[23]. Vestergaard P, Mosekilde L, Hyperthyroidism, bone mineral, and fracture risk–a meta-analysis, Thyroid 13 (6) (2003) 585–593. [PubMed: 12930603]

[24]. Rabinowitz MB, Toxicokinetics of bone lead, Environ. Health Perspect 91 (1991) 33–37. [PubMed: 2040248]

[25]. Pounds JG, Long GJ, Rosen JF, Cellular and molecular toxicity of lead in bone, Environ. Health Perspect 91 (1991) 17–32. [PubMed: 2040247]

[26]. Nash D, Magder LS, Sherwin R, Rubin RJ, Silbergeld EK, Bone density-related predictors of blood lead level among peri- and postmenopausal women in the United States: the third National Health and Nutrition Examination Survey, 1988–1994, Am. J. Epidemiol 160 (9) (2004) 901–911. [PubMed: 15496543]

[27]. Machida M, Sun S-J, Oguma E, Kayama F, High bone matrix turnover predicts blood levels of lead among perimenopausal women, Environ. Res 109 (7) (2009) 880–886. [PubMed: 19595303]

[28]. Lanphear BP, Dietrich K, Auinger P, Cox C, Cognitive deficits associated with blood lead concentrations < 10 μg/dL in US children and adolescents, Public Health Rep 115 (6) (2000) 521–529. [PubMed: 11354334]

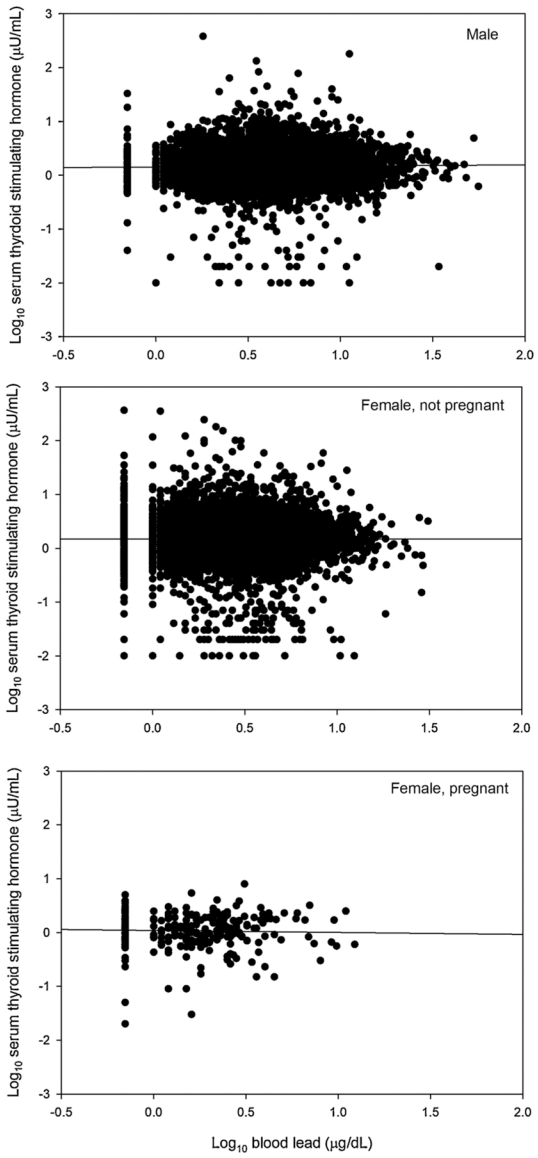

Fig. 1.

The relationship between $\log_{10}$ blood lead and $\log_{10}$ serum thyroid stimulating hormone by sex.

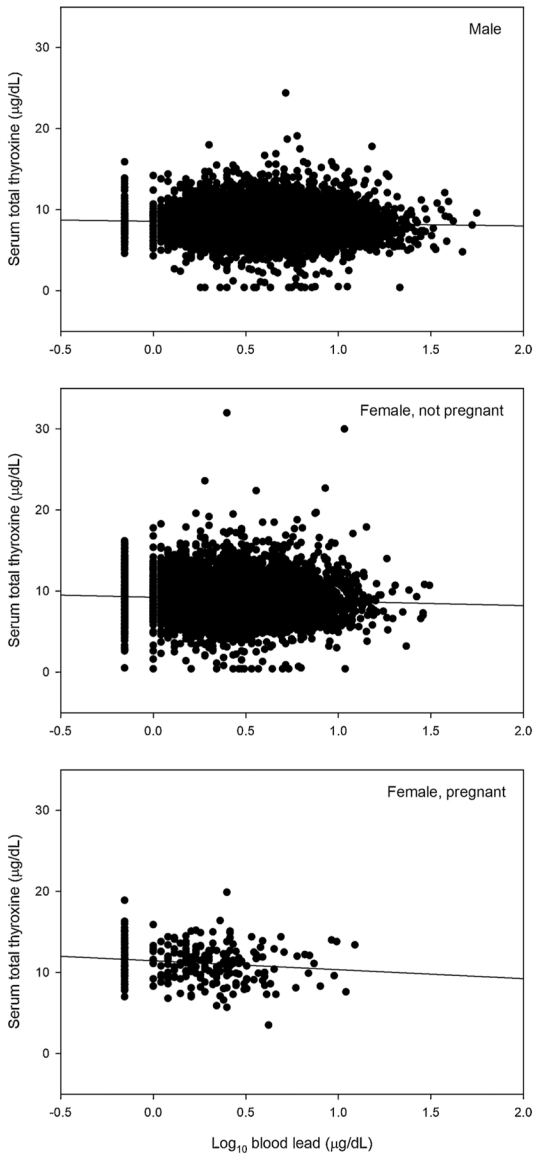

Fig. 2.

The relationship between $\log_{10}$ blood lead and serum total thyroxine by sex.

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Table 1

Estimates of the population means of the continuous variables.

Variable	n	Mean	SE	LCL	UCL	Minimum	Maximum
Body mass index	16523	26.52	0.11	26.30	26.74	11.7	79.6
Blood lead (μg/dL)	15932	3.55	0.10	3.35	3.75	0.7	56.0
Urinary creatinine (mg/dL)	16072	128.97	1.36	126.23	131.70	7.9	588.2
Urinary iodine (μg/dL)	15966	23.91	2.27	19.35	28.47	0.1	11000.0
Serum cotinine (ng/mL)	15533	77.894	2.541	72.789	83.000	0.035	1890.00
Serum thyroid stimulating hormone (μU/mL)	15313	2.112	0.057	1.998	2.225	0.00	382.00
Serum total thyroxine (μg/dL)	15194	8.76	0.06	8.64	8.87	0.4	32.0
Serum antimicrosomal antibody (U/mL)	15313	9.21	0.66	7.89	10.54	0.3	3000.0
Serum anti-thyroglobulin antibody (U/mL)	15313	6.71	0.89	4.92	8.50	0.7	3000.0
Total bone mineral density (g/cm^2)	14644	0.9436	0.0030	0.9376	0.9497	0.274	1.983
Length of fast (hours)	16229	10.716	0.072	10.572	10.860	0.00	39.13

SE: standard error.

LCL: lower 95% confidence limit.

UCL: upper 95% confidence limit.

Table 2

Estimates of the population mean concentrations of the thyroid hormones by classification variables.

Variable	Serum thyroid stimulating hormone (μU/mL)					Serum total thyroxine (μg/dL)				
Level	**n**	**Mean**	**SE**	**LCL**	**UCL**	**n**	**Mean**	**SE**	**LCL**	**UCL**
Race-ethnicity										
Non-Hispanic white	6371	2.154	0.058	2.039	2.270	6326	8.72	0.06	8.59	8.85
Non-Hispanic black	4120	1.755	0.183	1.388	2.123	4163	8.62	0.06	8.50	8.73
Mexican-American	4207	2.093	0.144	1.804	2.382	4081	9.13	0.05	9.03	9.24
Other	615	2.176	0.302	1.569	2.782	624	9.07	0.12	8.83	9.32
Sex										
Male	7174	1.909	0.065	1.778	2.040	7058	8.39	0.06	8.27	8.52
Female	8139	2.298	0.093	2.112	2.484	8136	9.09	0.06	8.96	9.22
Age group										
20–29	3237	1.541	0.035	1.472	1.611	3258	9.13	0.09	8.95	9.31
30–39	3080	1.808	0.096	1.615	2.000	3101	8.82	0.09	8.63	9.00
40–49	2422	2.146	0.113	1.918	2.374	2435	8.62	0.08	8.47	8.78
50–59	1739	2.484	0.213	2.056	2.913	1714	8.63	0.09	8.45	8.81
60–69	2147	2.532	0.107	2.318	2.747	2065	8.53	0.08	8.37	8.69
70–79	1586	3.031	0.203	2.624	3.438	1536	8.52	0.09	8.35	8.70
80–89	1013	2.826	0.147	2.531	3.121	999	8.44	0.08	8.28	8.61
90-	89	3.481	0.635	2.205	4.758	86	7.89	0.20	7.48	8.30
Session										
Morning	7561	2.207	0.083	2.040	2.375	7501	8.72	0.06	8.60	8.84
Afternoon	5057	2.023	0.074	1.874	2.172	5010	8.81	0.09	8.63	8.98
Evening	2695	2.017	0.101	1.814	2.219	2683	8.77	0.08	8.60	8.93
Pregnant										
No	7855	2.327	0.096	2.134	2.520	7850	9.02	0.07	8.89	9.15
Yes	261	1.458	0.074	1.308	1.607	263	11.32	0.21	10.90	11.74
Menopause										
No	4478	1.919	0.072	1.773	2.064	4504	9.18	0.07	9.04	9.32
Yes	2998	2.865	0.190	2.482	3.248	2968	8.84	0.08	8.68	9.00

Variable	Serum thyroid stimulating hormone (μU/mL)					Serum total thyroxine (μg/dL)				
Level	**n**	**Mean**	**SE**	**LCL**	**UCL**	**n**	**Mean**	**SE**	**LCL**	**UCL**
Surgical	663	2.828	0.253	2.320	3.337	664	9.37	0.17	9.04	9.71
Hormone pill use										
No	7633	2.250	0.095	2.059	2.441	7626	9.01	0.06	8.88	9.14
Yes	484	2.891	0.295	2.297	3.484	488	10.08	0.18	9.72	10.45
Vaginal cream use										
No	8045	2.294	0.094	2.106	2.482	8041	9.10	0.06	8.97	9.23
Yes	83	2.557	0.248	2.060	3.055	84	8.48	0.27	7.94	9.02
Hormone patch use										
No	8100	2.299	0.093	2.113	2.486	8097	9.09	0.06	8.96	9.22
Yes	37	2.065	0.195	1.672	2.457	37	8.36	0.35	7.66	9.06
Goiter										
No	15089	2.096	0.056	1.984	2.208	14975	8.74	0.06	8.63	8.85
Yes	222	3.237	0.720	1.789	4.684	217	10.13	0.31	9.50	10.75
Other thyroid disease										
No	14735	2.033	0.056	1.921	2.145	14615	8.71	0.06	8.60	8.82
Yes	576	3.857	0.637	2.577	5.136	577	9.75	0.19	9.38	10.12
Thyroid drug use										
No	14682	2.089	0.059	1.970	2.208	14566	8.70	0.06	8.58	8.81
Yes	469	2.854	0.305	2.240	3.468	466	10.37	0.22	9.93	10.82

SE: standard error.

LCL: lower 95% confidence limit.

UCL: upper 95% confidence limit.

Table 3

Estimated regression coefficients (slopes) for the continuous variables included in the linear regression models.

Dependent variable						
Independent variable	**Estimate**	**SE**	**LCL**	**UCL**	**t**	**p**
Log_{10} serum thyroid stimulating hormone (μU/mL)						
Age (years)	0.00268	0.00030	0.00208	0.00328	9.00	0.0000
Body mass index	0.00323	0.00096	0.00129	0.00517	3.35	0.0016
Log_{10} blood lead (μg/dL)	−0.02115	0.04058	−0.10270	0.06039	−0.52	0.6045
Urinary creatinine (mg/dL)	−0.00006	0.00005	−0.00016	0.00005	−1.06	0.2953
Log_{10} urinary iodine (μg/dL)	0.02195	0.01089	0.00006	0.04384	2.01	0.0494
Log_{10} serum cotinine (ng/mL)	−0.01837	0.00314	−0.02468	−0.01205	−5.85	0.0000
Serum total thyroxine (μg/dL)	−0.02729	0.00254	−0.03240	−0.02219	−10.74	0.0000
Log_{10} serum antimicrosomal antibody (U/mL)	0.12276	0.00913	0.10441	0.14111	13.45	0.0000
Log_{10} serum anti-thyroglobulin antibody (U/mL)	0.03170	0.01746	−0.00340	0.06679	1.81	0.0757
Total bone mineral density (g/cm^2)	0.08925	0.03106	0.02684	0.15166	2.87	0.0060
Length of fast (hours)	−0.00325	0.00098	−0.00522	−0.00129	−3.33	0.0017
Serum total thyroxine (μg/dL)						
Age (years)	−0.0152	0.0022	−0.0197	−0.0108	−6.94	0.0000
Body mass index	0.0015	0.0045	−0.0074	0.0105	0.35	0.7297
Log_{10} blood lead (μg/dL)	−0.8918	0.2030	−1.2998	−0.4838	−4.39	0.0000
Urinary creatinine (mg/dL)	0.0010	0.0005	0.0001	0.0019	2.12	0.0391
Log_{10} urinary iodine (μg/dL)	−0.2262	0.0947	−0.4164	−0.0359	−2.39	0.0208
Log_{10} serum cotinine (ng/mL)	0.0185	0.0183	−0.0183	0.0553	1.01	0.3178
Log_{10} serum antimicrosomal antibody (U/mL)	−0.2158	0.0672	−0.3508	−0.0808	−3.21	0.0023
Log_{10} serum anti-thyroglobulin antibody (U/mL)	−0.1183	0.1141	−0.3475	0.1109	−1.04	0.3048
Total bone mineral density (g/cm^2)	−1.0870	0.2223	−1.5337	−0.6403	−4.89	0.0000
Length of fast (hours)	0.0085	0.0095	−0.0105	0.0276	0.90	0.3718

SE: standard error.

LCL: lower 95% confidence limit.

UCL: upper 95% confidence limit.

For serum thyroid stimulating hormone, n = 12,963.

For serum total thyroxine, n = 13,009.

Denominator degrees of freedom = 49.

Table 4

Estimated regression coefficients (slopes) for the sex × pregnant × $\log_{10}$ blood lead (μg/dL) interaction.

Dependent variable							Interaction	
Level of sex × pregnant	**Estimate**	**SE**	**Lower**	**Upper**	**t**	**p**	**F**	**p**
Log_{10} serum thyroid stimulating hormone (μU/mL)								
Male	0.00574	0.02162	−0.03770	0.04919	0.27	0.7916	0.93	0.4006
Female, not pregnant	−0.03823	0.02271	−0.08388	0.00742	−1.68	0.0987		
Female, pregnant	−0.03098	0.11360	−0.25940	0.19740	−0.27	0.7863		
Serum total thyroxine (μg/dL)								
Male	−0.1495	0.1623	−0.4756	0.1766	−0.92	0.3614	7.02	0.0021
Female, not pregnant	−0.5199	0.1532	−0.8278	−0.2120	−3.39	0.0014		
Female, pregnant	−2.0060	0.5381	−3.0874	−0.9245	−3.73	0.0005		

SE: standard error.

LCL: lower 95% confidence limit.

UCL: upper 95% confidence limit.

For serum thyroid stimulating hormone, n = 12,963.

For serum total thyroxine, n = 13,009.

Denominator degrees of freedom = 49.

Table 5

Lowest blood lead concentration at which a relationship could be detected by level of sex × pregnant.

Dependent variable Level of sex × pregnant	Blood lead (μg/dL)	Estimate	SE	LCL	UCL	t	p
Serum total thyroxine (μg/dL)							
Female, not pregnant	2.1	−0.6896	0.3116	−1.3158	−0.0635	−2.21	0.0316
Female, pregnant	3.9	−1.5580	0.6671	−2.8986	−0.2174	−2.34	0.0237

SE: standard error.

LCL: lower 95% confidence limit.

UCL: upper 95% confidence limit.

For serum total thyroxine, n = 13,009.

Denominator degrees of freedom = 49.