

Thyroid Deficiency
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ABSTRACTS

ADVANCEDATA. National Center for Health Statistics.

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Vital & Health Statistics of the U S Department of Health and Education Welfare I. 1977;February 22, 1977 No. 5

Use of soy protein supplement and resultant need for increased dose of levothyroxine.

Bell DS, Ovalle F.

Endocr Pract. 2001 May; 7(3):193-4.

OBJECTIVE: To report a case of difficulty in achieving suppressive serum levels of thyroid hormone because of malabsorption of exogenous levothyroxine attributable to daily ingestion in close temporal relationship to the intake of a soy protein-containing food supplement. **METHODS:** We present the relevant history and laboratory data of the current case and provide supportive documentation from the literature. **RESULTS:** A 45-year-old woman who had hypothyroidism after a near-total thyroidectomy and radioactive iodine ablative therapy for papillary carcinoma of the thyroid required unusually high oral doses of levothyroxine to achieve suppressive serum levels of free thyroxine (T₄) and thyrotropin (thyroid-stimulating hormone or TSH). She had routinely been taking a "soy cocktail" protein supplement immediately after her levothyroxine. Temporal separation of the intake of the soy protein cocktail from the administration of the levothyroxine resulted in attainment of suppressive serum levels of free T₄ and TSH with use of lower doses of levothyroxine. **CONCLUSION:** Administration of levothyroxine concurrently with a soy protein dietary supplement results in decreased absorption of levothyroxine and the need for higher oral doses of levothyroxine to attain therapeutic serum thyroid hormone levels

Effects of thyroxine as compared with thyroxine plus triiodothyronine in patients with hypothyroidism.

Bunevicius R, Kazanavicius G, Zalinkevicius R, et al.

N Engl J Med. 1999 Feb 11; 340(6):424-9.

BACKGROUND: Patients with hypothyroidism are usually treated with thyroxine (levothyroxine) only, although both thyroxine and triiodothyronine are secreted by the normal thyroid gland. Whether thyroid secretion of triiodothyronine is physiologically important is unknown. **METHODS:** We compared the effects of thyroxine alone with those of thyroxine plus triiodothyronine (liothyronine) in 33 patients with hypothyroidism. Each patient was studied for two five-week periods. During one period, the patient received his or her usual dose of thyroxine. During the other, the patient received a regimen in which 50 microg of the usual dose of thyroxine was replaced by 12.5 microg of triiodothyronine. The order in which each patient received the two treatments was randomized. Biochemical, physiologic, and psychological tests were performed at the end of each treatment period. **RESULTS:** The patients had lower serum free and total thyroxine concentrations and higher serum total triiodothyronine concentrations after treatment with thyroxine plus triiodothyronine than after thyroxine alone, whereas the serum thyrotropin concentrations were similar after both treatments. Among 17 scores on tests of cognitive performance and assessments of mood, 6 were better or closer to normal after treatment with thyroxine plus triiodothyronine. Similarly, among 15 visual-analogue scales used to indicate mood and physical status, the results for 10 were significantly better after treatment with thyroxine plus triiodothyronine. The pulse rate and serum sex hormone-binding globulin concentrations were slightly higher after treatment with thyroxine plus triiodothyronine, but blood pressure, serum lipid concentrations, and the results of neurophysiologic tests were similar after the two treatments. **CONCLUSIONS:** In patients with hypothyroidism, partial substitution of triiodothyronine for thyroxine may improve mood and neuropsychological function; this finding suggests a specific effect of the triiodothyronine normally secreted by the thyroid gland

Homocysteine, hypothyroidism, and effect of thyroid hormone replacement.

Catargi B, Parrot-Roulaud F, Cochet C, et al.

Thyroid. 1999 Dec; 9(12):1163-6.

Elevation of total plasma concentration of homocysteine (t-Hcy) is an important and independent risk factor for cardiovascular disease. Hypothyroidism is possibly also associated with an increased risk for coronary artery disease, which may be related to atherogenic changes in lipid profile. Because hypothyroidism decreases hepatic levels of enzymes involved in the remethylation pathway of homocysteine, we prospectively evaluated fasting and postload t-Hcy in patients before and after recovery of euthyroidism. Fasting and postload t-Hcy levels were higher in 40 patients with peripheral hypothyroidism (14 with autoimmune thyroiditis and 26 treated for thyroid cancer) in comparison with those of 26 controls (13.0 +/- 7.5 vs. 8.5 +/- 2.6 micromol/L, $p < .01$, respectively, and 49.9 +/- 37.3 vs. 29.6 +/- 8.4 micromol/L $p < .001$, respectively). On univariate analysis, fasting Hcy was positively related to thyrotropin (TSH) and inversely related to folates. Multivariate analysis confirmed TSH as the strongest predictor of t-Hcy independent of age, folate, vitamin B12, and creatinine. Thyroid hormone replacement significantly decreased fasting but not postload t-Hcy. We conclude that t-Hcy is elevated in hypothyroidism. The association of hyperhomocysteinemia and lipid abnormalities occurring in hypothyroidism may represent a dynamic atherogenic state. Thyroid hormone failed to completely normalize t-Hcy. Potential benefit of treatment with folic acid in combination with thyroid hormone replacement has to be tested given that hypothyroid patients were found to have lower levels of folate

Selenium decreases thyroglobulin concentrations but does not affect the increased thyroxine-to-triiodothyronine ratio in children with congenital hypothyroidism.

Chanoine JP, Neve J, Wu S, et al.

J Clin Endocrinol Metab. 2001 Mar; 86(3):1160-3.

Compared with euthyroid controls, patients with congenital hypothyroidism (CH) who are receiving L-T(4) treatment show elevated serum TSH relative to serum T(4) concentrations and increased T(4)/T(3) ratio. These abnormalities could be the consequence of impaired activity of the selenoenzymes deiodinases on which patients with CH rely to convert the ingested L-T(4) into active T(3). Eighteen patients (0.5-15.4 yr), diagnosed with CH in infancy, received selenomethionine (SeM, 20-60 microg selenium/day) for 3 months. The study took place in Belgium, a country where selenium intake is borderline. Compared with the values observed in age- and sex-matched euthyroid controls, patients with CH had decreased selenium, thyroglobulin and T(3) concentrations and increased TSH, reverse T(3), and T(4) concentrations and T(4)/T(3) ratio at baseline. Selenium supplementation caused a 74% increase in plasma selenium values but did not affect the activity of the selenoenzyme glutathione peroxidase used as a marker of selenium status. SeM abolished the TSH difference observed between CH patients and euthyroid controls at baseline and caused a significant decrease in thyroglobulin values. Thyroid hormone concentrations were not affected by SeM. In conclusion, our data suggest that selenium is not a limiting factor for peripheral T(4)-to-T(3) conversion in CH patients. In contrast, we find indirect evidence that SeM improves thyroid hormones feedback at the hypothalamo-pituitary level and decreases stimulation of the residual thyroid tissue, possibly suggesting greater intracellular T(4)-to-T(3) conversion

Effects of selenium deficiency on thyroid necrosis, fibrosis and proliferation: a possible role in myxoedematous cretinism.

Contempre B, Dumont JE, Deneff JF, et al.

Eur J Endocrinol. 1995 Jul; 133(1):99-109.

It has been suggested that selenium deficiency is a co-factor to iodine deficiency in the pathogenesis of myxoedematous cretinism. The mechanism proposed is that the generation of hydrogen peroxide is greatly increased in iodine-deficient thyroid glands, and that selenium is involved in the control of hydrogen peroxide and its derived free radicals. This study was carried out to investigate the effect of the possibly impaired cellular defence mechanism associated with selenium deficiency on thyroid necrosis and tissue repair. For this purpose, we studied thyroid tissue from selenium- (SE-) and/or iodine-deficient (I-) rats before and after an acute toxic iodine overload. In I- thyroids, necrotic cells were numerous. Acute iodine administration increased this effect. Necrosis was associated with transient infiltration of inflammatory cells. In I-SE+ thyroids the tissue resumed its normal appearance. In I-SE- thyroid glands, the iodide toxicity was stronger, with greater necrosis and inflammatory reaction. The inflammation resolved but was replaced by fibrotic tissue. Fifteen days after the toxic overload, the connective tissue volume was twice the control value. Before iodide overload, the proportion of dividing cells was equal in I-SE+ and I-SE- thyroids. Three days after the iodide overload, this proportion was increased in I-SE+ thyroids but reduced in the I-SE- thyroids. Overall, the I-SE- thyroids had four times fewer dividing cells than the I-SE+ thyroids. In summary, selenium deficiency coupled to iodine deficiency increased necrosis, induced fibrosis and impeded compensatory epithelial cell proliferation. These results are compatible with histological and functional description of thyroid tissue from myxoedematous cretins

Whose normal thyroid function is better--yours or mine?

Dayan CM, Saravanan P, Bayly G.

Lancet. 2002 Aug 3; 360(9330):353.

Determinants of changes in plasma homocysteine in hyperthyroidism and hypothyroidism.

Diekman MJ, van der Put NM, Blom HJ, et al.

Clin Endocrinol (Oxf). 2001 Feb; 54(2):197-204.

OBJECTIVE: Hyperhomocysteinaemia is a risk factor for premature atherosclerotic vascular disease and venous thrombosis. The aim of the present study was to assess plasma total homocysteine (tHCys) concentrations in hypo- as well as hyperthyroid patients before and after treatment, and to evaluate the role of potential determinants of plasma tHCys levels in these patients. **DESIGN:** Prospective follow up study. **PATIENTS:** Fifty hypothyroid and 46 hyperthyroid patients were studied in the untreated state and again after restoration of euthyroidism. **MEASUREMENTS:** Fasting plasma levels of tHCys and its putative determinants (plasma levels of free thyroxine (fT4), folate, vitamin B(12), renal function, sex, age, smoking status and the C677T polymorphism in the methylenetetrahydrofolate reductase (MTHFR) gene) were measured before and after treatment. **RESULTS:** Restoration of the euthyroid state decreased both tHCys (17.6 +/- 10.2-13.0 +/- 4.7 micromol/l; P < 0.005) and creatinine (83.9 +/- 22.0-69.8 +/- 14.2 micromol/l; P < 0.005) in hypothyroid patients and increased both tHCys (10.7 +/- 2.5-13.4 +/- 3.3 micromol/l; P < 0.005) and creatinine (49.0 +/- 15.4-66.5 +/- 15.0 micromol/l; P < 0.005) in hyperthyroid patients (values as mean +/- SD). Folate levels were lower in the hypothyroid group compared to the hyperthyroid group (11.7 +/- 6.4 and 15.1 +/- 7.6 nmol/l; P < 0.05). Pretreatment tHCys levels correlated with log fT(4) (r = - 0.47), folate (r = - 0.21), plasma creatinine (r = 0.45) and age (r = 0.35) but not with C677T genotype. Multivariate analysis indicated that pretreatment log(fT(4)) levels and age accounted for 28% the variability of pre-treatment tHCys (tHCys = 14.2-5.50 log(fT(4)) + 0.14 age). After treatment the logarithm of the change (Delta) in fT(4) (expressed as the post-treatment fT(4)/pre-treatment fT(4) ratio) accounted for 45% of the variability in change of tHCys (tHCys = - 0.07-4.94 log (fT(4))); there was no independent contribution of changes in creatinine which was, however, strongly related to changes in tHCys (r = 0.61). **CONCLUSIONS:** Plasma tHCys concentrations increased in hypothyroidism and decreased in hyperthyroidism. Plasma fT(4) is an independent determinant of tHCys concentrations. Lower folate levels and a lower creatinine clearance in hypo-thyroidism, and a higher creatinine clearance in hyperthyroidism only partially explain the changes in tHCys

Anti-thyroid isoflavones from soybean: isolation, characterization, and mechanisms of action.

Divi RL, Chang HC, Doerge DR.

Biochem Pharmacol. 1997 Nov 15; 54(10):1087-96.

The soybean has been implicated in diet-induced goiter by many studies. The extensive consumption of soy products in infant formulas and in vegetarian diets makes it essential to define the goitrogenic potential. In this report, it was observed that an acidic methanolic extract of soybeans contains compounds that inhibit thyroid peroxidase- (TPO) catalyzed reactions essential to thyroid hormone synthesis. Analysis of the soybean extract using HPLC, UV-VIS spectrophotometry, and LC-MS led to identification of the isoflavones genistein and daidzein as major components by direct comparison with authentic standard reference isoflavones. HPLC fractionation and enzymatic assay of the soybean extract showed that the components responsible for inhibition of TPO-catalyzed reactions coeluted with daidzein and genistein. In the presence of iodide ion, genistein and daidzein blocked TPO-catalyzed tyrosine iodination by acting as alternate substrates, yielding mono-, di-, and triiodoisoflavones. Genistein also inhibited thyroxine synthesis using iodinated casein or human goiter thyroglobulin as substrates for the coupling reaction. Incubation of either isoflavone with TPO in the presence of H₂O₂ caused irreversible inactivation of the enzyme; however, the presence of iodide ion in the incubations completely abolished the inactivation. The IC₅₀ values for inhibition of TPO-catalyzed reactions by genistein and daidzein were ca. 1-10 microM, concentrations that approach the total isoflavone levels (ca. 1 microM) previously measured in plasma from humans consuming soy products. Because inhibition of thyroid hormone synthesis can induce goiter and thyroid neoplasia in rodents, delineation of anti-thyroid mechanisms for soy isoflavones may be important for extrapolating goitrogenic hazards identified in chronic rodent bioassays to humans consuming soy products

Breast feeding and insulin-dependent diabetes mellitus in children.

Fort P, Lanes R, Dahlem S, et al.

J Am Coll Nutr. 1986; 5(5):439-41.

We have evaluated the hypothesis of a protective effect of human milk on the development of insulin dependent diabetes mellitus

(IDDM). We studied the feeding histories of 95 diabetic children and compared them with controls consisting of their non-diabetic siblings and a pair matched group of nondiabetic peers of the same age, sex, geographical location, and social background. The incidence of breast feeding in diabetic children was 18%. This was similar to the control group. The duration of breast feedings was also similar among all three groups. There was no difference in the age of introduction of solid food between diabetic and nondiabetic children. Twice as many diabetic children, however, received soy containing formula in infancy as compared to control children. The mean age of onset of IDDM was not related to the type of feeding during infancy. The incidence of positive thyroid antibodies was two and one half times higher in formula-fed diabetic children than in breast-fed ones. In our studies we were unable to document any relationship between the history of breast feeding and subsequent development of IDDM in children

Breast and soy-formula feedings in early infancy and the prevalence of autoimmune thyroid disease in children.

Fort P, Moses N, Fasano M, et al.

J Am Coll Nutr. 1990 Apr; 9(2):164-7.

It has been suggested that feeding practices in infancy may affect the development of various autoimmune diseases later in life. Since thyroid alterations are among the most frequently encountered autoimmune conditions in children, we studied whether breast and soy-containing formula feedings in early life were associated with the subsequent development of autoimmune thyroid disease. A detailed history of feeding practices was obtained in 59 children with autoimmune thyroid disease, their 76 healthy siblings, and 54 healthy nonrelated control children. There was no difference in the frequency and duration of breast feeding in early life among the three groups of children. However, the frequency of feedings with soy-based milk formulas in early life was significantly higher in children with autoimmune thyroid disease (prevalence 31%) as compared with their siblings (prevalence 12%; $\chi^2 = 7.22$ with continuity factor; p less than 0.01), and healthy nonrelated control children (prevalence 13%, $\chi^2 = 5.03$ with continuity factor; p less than 0.02). Therefore, this retrospective analysis documents the association of soy formula feedings in infancy and autoimmune thyroid disease

Inhibition of proliferation and expression of T1 and cyclin D1 genes by thyroid hormone in mammary epithelial cells.

Gonzalez-Sancho JM, Figueroa A, Lopez-Barahona M, et al.

Mol Carcinog. 2002 May; 34(1):25-34.

The relationship between thyroid hormone (triiodothyronine, T(3)) and breast cancer is unclear. We studied the effect of the c-erbA/TR alpha proto-oncogene encoding a functional T(3) receptor (TR alpha 1), of its ligand T(3), and of its retroviral, mutated counterpart, the v-erbA oncogene, on the proliferation capacity of nontumorigenic mammary epithelial cells (EpH4). We found that EpH4 cells expressing ectopically TR (Eph4 + TR alpha 1) or v-erbA (Eph4 + v-erbA) proliferated faster than parental EpH4 cells that contained low levels of endogenous TR. T(3) inhibited DNA synthesis and proliferation in Eph4 + TR alpha 1 cells but not Eph4 or Eph4 + v-erbA cells. The study of cell-cycle genes showed that T(3) decreased cyclin D1 RNA and protein levels in Eph4 + TR alpha 1 cells. In addition, T(3) downregulated the expression of T1, a gene that is overexpressed in human breast adenocarcinomas and is induced by mitogens, serum, and several oncogenes and cytokines. Inhibition of the T1 gene by T(3) required both de novo mRNA and protein synthesis. Furthermore, T(3) abolished the induction of T1 by the tumor promoter 12-O-tetradecanoylphorbol-13-acetate and inhibited the activity of an activation protein 1-dependent promoter (-73-Col-CAT) in Eph4 + TR alpha 1 cells, suggesting that interference with activation protein 1 transcription factor plays a part in the inhibition of the T1 gene. Our results showed that T(3) reduced the proliferation of mammary epithelial cells and inhibited the expression of cyclin D1 and T1 genes

Does low tri-iodothyronine independently predict mortality in elderly hospitalised patients?

Gupta A, Haboubi N, Thomas P.

Int J Clin Pract. 2001 Jul; 55(6):409-10.

A fall in serum tri-iodothyronine (T3) is the earliest abnormality in thyroid hormonal function tests in non-thyroidal illnesses. Our study shows an association of low serum T3 with patient mortality in elderly hospitalised patients

Low headache prevalence amongst women with high TSH values.

Hagen K, Bjoro T, Zwart JA, et al.

Eur J Neurol. 2001 Nov; 8(6):693-9.

The aim of this large cross-sectional population-based study was to examine a possible positive or negative association between thyroid dysfunction and headache. Between 1995 and 1997, all 92 566 adults in Nord-Trøndelag County in Norway were invited to participate in a health survey. A total of 51 383 (56%) responded to a headache questionnaire, whereof thyroid-stimulating hormone (TSH) was measured in 28 058 individuals. These included 15 465 women and 8019 men above 40 years of age, 1767 randomly selected individuals between 20 and 40 years of age, and 2807 (97%) with thyroid dysfunction. Associations between thyroid dysfunction and headache were assessed in multivariate analyses, estimating prevalence odds ratios (OR) with 95% confidence intervals (CIs). High TSH values were associated with low prevalence of headache. This was most evident amongst women with no history of thyroid dysfunction. Amongst these, headache was less probable (OR=0.5, 95% CI 0.3-0.7) if TSH > or = 10 mU/l than in women with normal TSH (0.2-4 mU/l). In all age groups between 40 and 80 years, TSH was lower amongst headache sufferers, especially migraineurs, than in those without headache complaints

Subclinical hypothyroidism is an independent risk factor for atherosclerosis and myocardial infarction in elderly women: the Rotterdam Study.

Hak AE, Pols HA, Visser TJ, et al.

Ann Intern Med. 2000 Feb 15; 132(4):270-8.

BACKGROUND: Overt hypothyroidism has been found to be associated with cardiovascular disease. Whether subclinical hypothyroidism and thyroid autoimmunity are also risk factors for cardiovascular disease is controversial. **OBJECTIVE:** To investigate whether subclinical hypothyroidism and thyroid autoimmunity are associated with aortic atherosclerosis and myocardial infarction in postmenopausal women. **DESIGN:** Population-based cross-sectional study. **SETTING:** A district of Rotterdam, The Netherlands. **PARTICIPANTS:** Random sample of 1149 women (mean age +/- SD, 69.0 +/- 7.5 years) participating in the Rotterdam Study. **MEASUREMENTS:** Data on thyroid status, aortic atherosclerosis, and history of myocardial infarction were obtained at baseline. Subclinical hypothyroidism was defined as an elevated thyroid-stimulating hormone level (>4.0 mU/L) and a normal serum free thyroxine level (11 to 25 pmol/L [0.9 to 1.9 ng/dL]). In tests for antibodies to thyroid peroxidase, a serum level greater than 10 IU/mL was considered a positive result. **RESULTS:** Subclinical hypothyroidism was present in 10.8% of participants and was associated with a greater age-adjusted prevalence of aortic atherosclerosis (odds ratio, 1.7 [95% CI, 1.1 to 2.6]) and myocardial infarction (odds ratio, 2.3 [CI, 1.3 to 4.0]). Additional adjustment for body mass index, total and high-density lipoprotein cholesterol level, blood pressure, and smoking status, as well as exclusion of women who took beta-blockers, did not affect these estimates. Associations were slightly stronger in women who had subclinical hypothyroidism and antibodies to thyroid peroxidase (odds ratio for aortic atherosclerosis, 1.9 [CI, 1.1 to 3.6]; odds ratio for myocardial infarction, 3.1 [CI, 1.5 to 6.3]). No association was found between thyroid autoimmunity itself and cardiovascular disease. The population attributable risk percentage for subclinical hypothyroidism associated with myocardial infarction was within the range of that for known major risk factors for cardiovascular disease. **CONCLUSION:** Subclinical hypothyroidism is a strong indicator of risk for atherosclerosis and myocardial infarction in elderly women

Effects of intensive blood-pressure lowering and low-dose aspirin in patients with hypertension: principal results of the Hypertension Optimal Treatment (HOT) randomised trial. HOT Study Group.

Hansson L, Zanchetti A, Carruthers SG, et al.

Lancet. 1998 Jun 13; 351(9118):1755-62.

BACKGROUND: Despite treatment, there is often a higher incidence of cardiovascular complications in patients with hypertension than in normotensive individuals. Inadequate reduction of their blood pressure is a likely cause, but the optimum target blood pressure is not known. The impact of acetylsalicylic acid (aspirin) has never been investigated in patients with hypertension. We aimed to assess the optimum target diastolic blood pressure and the potential benefit of a low dose of acetylsalicylic acid in the treatment of hypertension. **METHODS:** 18790 patients, from 26 countries, aged 50-80 years (mean 61.5 years) with hypertension and diastolic blood pressure between 100 mm Hg and 115 mm Hg (mean 105 mm Hg) were randomly assigned a target diastolic blood pressure. 6264 patients were allocated to the target pressure < or =90 mm Hg, 6264 to < or =85 mm Hg, and 6262 to < or =80 mm Hg. Felodipine was given as baseline therapy with the addition of other agents, according to a five-step regimen. In addition, 9399 patients were randomly assigned 75 mg/day acetylsalicylic acid (Bamcor, Astra) and 9391 patients were assigned placebo. **FINDINGS:** Diastolic blood pressure was reduced by 20.3 mm Hg, 22.3 mm Hg, and 24.3 mm Hg, in the < or =90 mm Hg, < or =85 mm Hg, and < or =80 mm Hg target groups, respectively. The lowest incidence of major cardiovascular events occurred at a mean achieved diastolic blood pressure of 82.6 mm Hg; the lowest risk of cardiovascular mortality occurred at 86.5 mm Hg. Further reduction below these blood pressures was safe. In patients with diabetes mellitus there was a 51% reduction in major cardiovascular events in target group < or =80 mm Hg compared with target group < or =90 mm Hg (p for trend=0.005). Acetylsalicylic acid reduced major cardiovascular events by 15% (p=0.03) and all myocardial infarction by 36% (p=0.002), with no effect on stroke. There were seven fatal bleeds in the acetylsalicylic acid group and eight in the placebo group, and 129 versus 70 non-fatal major bleeds in the two groups, respectively (p<0.001). **INTERPRETATION:** Intensive lowering of blood pressure in patients with hypertension was associated with a low rate of

cardiovascular events. The HOT Study shows the benefits of lowering the diastolic blood pressure down to 82.6 mm Hg. Acetylsalicylic acid significantly reduced major cardiovascular events with the greatest benefit seen in all myocardial infarction. There was no effect on the incidence of stroke or fatal bleeds, but non-fatal major bleeds were twice as common

Normalization of hyperhomocysteinemia with L-thyroxine in hypothyroidism.

Hussein WI, Green R, Jacobsen DW, et al.

Ann Intern Med. 1999 Sep 7; 131(5):348-51.

BACKGROUND: Hyperhomocysteinemia is an independent risk factor for coronary, peripheral, and cerebrovascular disease. Elevated plasma homocysteine levels were described in a preliminary report on primary hypothyroidism. **OBJECTIVE:** To determine whether restoration of euthyroidism by L-thyroxine replacement therapy would reduce or normalize plasma homocysteine levels. **DESIGN:** Prospective cohort study. **SETTING:** Outpatient endocrinology department of a tertiary center. **PATIENTS:** 14 patients (10 women and 4 men; 25 to 77 years of age): 4 with newly diagnosed chronic (Hashimoto) hypothyroidism and 10 who had been rendered acutely hypothyroid (thyroid-stimulating hormone level > 25 mU/L) by total thyroidectomy for thyroid carcinoma. **MEASUREMENTS:** Total plasma homocysteine levels were measured at baseline and 3 to 9 months later, after euthyroidism had been attained by L-thyroxine replacement therapy. **RESULTS:** Median baseline plasma homocysteine levels in both sexes (women, 11.65 micromol/L [range, 7.2 to 26.5 micromol/L]; men, 15.1 micromol/L [range, 14.1 to 16.3 micromol/L]) were higher ($P = 0.002$) than those in healthy female ($n = 35$) and male ($n = 36$) volunteers (women, 7.52 micromol/L [range, 4.3 to 14.0 micromol/L]; men, 8.72 micromol/L [range, 5.94 to 14.98 micromol/L]). Eight patients (57%) had baseline plasma homocysteine levels that exceeded the upper limit of sex-specific reference ranges. Upon attainment of euthyroidism, all patients had a diminution in plasma homocysteine levels. The median overall change of -5.5 micromol/L (range, -15.4 to -1.8 micromol/L) corresponds to a difference of -44% (range, -58% to -13%) ($P < 0.001$). Homocysteine levels returned to normal in 7 of the 8 patients with elevated pretreatment values. **CONCLUSIONS:** Hypothyroidism may be a treatable cause of hyperhomocysteinemia, and elevated plasma homocysteine levels may be an independent risk factor for the accelerated atherosclerosis seen in primary hypothyroidism

[Treatment of euthyroid goiter in the elderly].

Imbrogno N, De Angelis G, Salandri A, et al.

Clin Ter. 2001 Jul; 152(4):231-4.

PURPOSE: A study was conducted to evaluate the effectiveness of the medical therapy with synthetic hormone levothyroxine (L-T4) in the elderly subjects with multinodular euthyroid goiter. **PATIENTS AND METHODS:** 187 elderly subjects (34 males and 153 females) ranging between 63 and 85 years of age with multinodular euthyroid goiter were examined. For each subject has been calculated the index of body mass (BMI) which has consented the identify two groups of subjects: the elderly patients with normal weight and the obese subjects. **RESULTS:** In the mostly of the patients (82%), both normal weight and obese, the L-T4 therapy has not determined significant changes either of the dimensions or the number of the nodules. In the obese subjects the L-T4 therapy has not caused decrease of weight at least to the 20% of the initial body weight. **CONCLUSIONS:** The results of the research have proved the limited effectiveness of the suppressive therapy with levothyroxine in the reduction of the volume and/or of the number of the nodules, without however denying the usefulness in the preventing the worsening of the nodular disease of thyroid. The study also has revealed that the therapy with levothyroxine is ineffective for the body weight reduction in the obese subjects

Abnormal thyroid function tests in infants with congenital hypothyroidism: the influence of soy-based formula.

Jabbar MA, Larrea J, Shaw RA.

J Am Coll Nutr. 1997 Jun; 16(3):280-2.

OBJECTIVE: To assess the etiology of hyperthyroxinemia or hyperthyrotropinemia in infants with congenital hypothyroidism who are on replacement therapy with L-thyroxine. **METHODS:** These infants were treated with recommended doses of L-thyroxine following the diagnosis of congenital hypothyroidism. Because of hyperthyroxinemia (2 patients) and hyperthyrotropinemia (1 patient), medication compliance and dietary practice (formula type, age of introduction, and discontinuation or change of the formula) were assessed. Clinical evaluation was also performed. **RESULTS:** Elevated thyroxine level in 2 infants was associated with discontinuation of soy formula 4 weeks previously; reduction of L-thyroxine dose normalized serum levels in both of these infants. In the third infant, who received soy formula from 1 week of age, TSH remained elevated despite incremental L-thyroxine doses of 19 micrograms/kg/day; discontinuation of soy formula was followed by normalization of the TSH in 3 weeks and helped attain a subsequent decrement of L-thyroxine dose to 8.6 micrograms/kg/day. Neither the hyperthyroxinemia nor hyperthyrotropinemia in these infants was associated with any adverse behavioral-developmental consequence. **CONCLUSION:**

When initiating soy-formula feeding in infants with congenital hypothyroidism, the L-thyroxine dose should be increased because of significant reduction in intestinal absorption: conversely, when soy feeding is discontinued, the L-thyroxine dose should be decreased

Thyroid disease and female reproduction.

Krassas GE.

Fertil Steril. 2000 Dec; 74(6):1063-70.

OBJECTIVE: To review the menstrual function and fertility in thyroid disease, mainly in hyperthyroidism and hypothyroidism. Also to register the consequences of (131)I therapy, which is used widely in the treatment of Graves' disease and thyroid cancer, on subsequent pregnancies and on fertility in these patients. DESIGN: A MEDLINE computer search was used to identify relevant studies. The type of menstrual disturbances and the status of fertility were recorded from all the studies found. Also, the fertility and genetic hazard of female patients with Graves' disease and thyroid cancer who were treated with (131)I were registered. RESULT(S): Both hyperthyroidism and hypothyroidism may result in menstrual disturbances. Menstrual abnormalities are less common now than in previous series. In a recent study, we found that only 21.5% of 214 thyrotoxic patients had some type of menstrual disturbance, compared to 50 to 60% in some older series. The most common manifestations are hypomenorrhea and oligomenorrhea. According to the results of endometrial biopsies, most thyrotoxic women remain ovulatory. Moreover, the genetic hazard incident to radioiodine therapy in Graves' disease and thyroid carcinoma is very small; exposure to (131)I does not cause reduced fecundity, and the risk of loss of fertility is not a contraindication for its use in these patients. In hypothyroidism, the frequency of menstrual irregularities has very recently been reported to be 23.4% among 171 hypothyroid patients studied. This is much less than that reported in previous studies, which showed that 50 to 70% of hypothyroid female patients had menstrual abnormalities. The most common manifestation is oligomenorrhea. Severe hypothyroidism is commonly associated with failure of ovulation. Ovulation and conception can occur in mild hypothyroidism. These pregnancies are, however, often associated with abortions, stillbirths, or prematurity. The latter may be of greater clinical importance in infertile women with unexplained infertility. CONCLUSION(S): These new data, mainly concerning menstrual abnormalities in hyperthyroidism and hypothyroidism, are inconsistent with what is generally believed and written in the classic thyroid textbooks and indicate that such opinions should be revised

[Effect of lead on thyroid function].

Lasisz B, Zdrojewicz Z, Marcinkowski Z.

Wiad Lek. 1992 Feb; 45(3-4):116-9.

Lead in organic and inorganic compounds is a health risk factor leading after high-grade exposure to poisoning. It can accumulate in the organism and exert toxic effects, especially on the haemopoietic system and nervous system. Its action includes damage to cell membranes and disorders of the oxidoreductive processes in the cells. Hypothyroidism occurring in subjects with occupational exposure to lead may evidence a negative effect of the element on thyroid function

Screening for hypothyroidism in infertile women.

Lincoln SR, Ke RW, Kutteh WH.

J Reprod Med. 1999 May; 44(5):455-7.

OBJECTIVE: To determine the frequency of an elevated thyroid-stimulating hormone (TSH) level in 704 patients seeking treatment for infertility. STUDY DESIGN: Sera from 704 women evaluated for infertility were assayed for TSH levels using radioimmunoassay (normal, 0.45-4.09 mIU/mL). All women had at least one year of infertility. Women with a known history of thyroid disease were excluded from the review. RESULTS: Sixteen of 704 patients (2.3%) had elevated TSH levels and were treated with levothyroxine to normalize TSH. None of these women had overt clinical signs or symptoms of hypothyroidism. Of these women, 11 of 16, or 69%, had ovulatory dysfunction, and 7 (64%) later became pregnant while on thyroid replacement. Five of 704 (0.7%) women with infertility who presented without a history of ovulatory dysfunction had elevated TSH levels, and none became pregnant with treatment. CONCLUSION: The prevalence of elevated TSH in 704 women with at least one year of infertility was 2.3%. The majority of women diagnosed with hypothyroidism (11 of 16, or 69%) had ovulatory dysfunction. With treatment for hypothyroidism, successful pregnancies resulted in 7 of 11 (64%) of patients. Women with infertility and ovulatory dysfunction should be screened for hypothyroidism. Screening for hypothyroidism as part of a routine infertility workup in women with normal ovulatory function will yield few abnormal tests

Homocysteine and restenosis after percutaneous coronary intervention.

Numerous clinical studies in Western and Asian countries suggest that individuals with elevated blood levels of homocysteine have an increased risk of atherosclerosis, myocardial infarction, cerebral infarction, and deep vein thrombosis. Homocysteine is also known to induce both atherogenic and thrombogenic mediators in cultured vascular cells so that homocysteine may influence the damage of endothelial cells, promote smooth muscle cell growth, induce atherogenic mediators and thrombus formation after coronary angioplasty. The association between homocysteine and restenosis after percutaneous coronary intervention (PCI) has been discussed. In this study, the relationship between plasma homocysteine levels and restenosis after PCI to investigate whether plasma homocysteine levels may be a predictor of restenosis after PCI was examined. One hundred consecutive patients who underwent successful PCI were enrolled and plasma homocysteine level was measured in all patients prior to PCI. Plasma homocysteine level was obtained in 99 of 100 patients who had angioplasty. The mean plasma homocysteine concentration in the enrolled patients was 13.61 +/- 6.04 micromol/L. The minimum and maximum of plasma homocysteine were 4.40 micromol/L and 50.00 micromol/L, respectively. In healthy subjects, the normal reference range of homocysteine level is 5-15 micromol/L. However, recent data suggest that some patients may be at increased cardiovascular and cerebrovascular risk at levels as low as 12 micromol/L. For this reason, both cut off points of homocysteine level > or = 15 micromol/L or > or = 12 micromol/L to identify the high homocysteine level group were used. Of 99 patients, high homocysteine level (> or = 15 micromol/L) was established in 9 patients with restenosis versus 20 patients without restenosis. If the cut off point of homocysteine level > or = 12 micromol/L was used, high homocysteine level was established in 14 patients with restenosis versus 39 patients without restenosis. From both cut off points of homocysteine level, there was no correlation between plasma homocysteine level and the restenosis group. (p>0.05)

Medical Nutrition from Marz.

Marz RB.

1997;

High serum cholesterol levels in persons with 'high-normal' TSH levels: should one extend the definition of subclinical hypothyroidism?

Michalopoulou G, Alevizaki M, Pipingos G, et al.

Eur J Endocrinol. 1998 Feb; 138(2):141-5.

OBJECTIVE: The association between established hypothyroidism and high cholesterol levels is well known. The aim of the present study was to investigate the effect of thyroxine (T4) administration on cholesterol levels in hypercholesterolemic subjects with TSH levels within the normal range ('high-normal' TSH compared with 'low-normal' TSH). **DESIGN AND METHODS:** We determined TSH levels in 110 consecutive patients referred for hypercholesterolemia (serum cholesterol >7.5 mmol/l). Those with 'high-normal' TSH (2.0-4.0 microU/ml) as well as those with 'low-normal' TSH (0.40-1.99 microU/ml) were randomly assigned to receive either 25 or 50 microg T4 daily for two months. Thus, groups A and B (low-normal TSH) received 25 and 50 microg T4 respectively and groups C and D (high-normal TSH) received 25 and 50 microg T4 respectively. Serum T4, tri-iodothyronine (T3), TSH, free thyroxine index, resin T3 uptake and thyroid autoantibodies (ThAab) as well as total cholesterol, high and low density lipoprotein cholesterol (HDL, LDL), and triglycerides were determined before and at the end of the two-month treatment period. **RESULTS:** TSH levels were reduced in all groups. The most striking effect was observed in group D (TSH levels before: 2.77 +/- 0.55, after: 1.41 +/- 0.85 microU/ml, P < 0.01). Subjects in groups C and D had a higher probability of having positive ThAabs. A significant reduction in total cholesterol (P < 0.01) and LDL (P < 0.01) was observed after treatment only in group D. In those subjects in group D who were ThAab negative, there was no significant effect of thyroxine on cholesterol levels. **CONCLUSIONS:** Subjects with high-normal TSH levels combined with ThAabs may, in fact, have subclinical hypothyroidism presenting with elevated cholesterol levels. It is possible that these patients might benefit from thyroxine administration

Plasma total homocysteine levels in hyperthyroid and hypothyroid patients.

Nedrebo BG, Ericsson UB, Nygard O, et al.

Metabolism. 1998 Jan; 47(1):89-93.

We found a higher plasma concentration of total homocysteine (tHcy), an independent risk factor for cardiovascular disease, in patients with hypothyroidism (mean, 16.3 micromol/L; 95% confidence interval [CI], 14.7 to 17.9 micromol/L) than in healthy controls (mean, 10.5 micromol/L; 95% CI, 10.1 to 10.9 micromol/L). The tHcy level of hyperthyroid patients did not differ

significantly from that of the controls. Serum creatinine was higher in hypothyroid patients and lower in hyperthyroid patients than in controls, whereas serum folate was higher in hyperthyroid patients compared with the two other groups. In multivariate analysis, these differences did not explain the higher tHcy concentration in hypothyroidism. We confirmed the observation of elevated serum cholesterol in hypothyroidism, which together with the hyperhomocysteinemia may contribute to an accelerated atherogenesis in these patients

Smoking--a risk factor for hypothyroidism.

Nystrom E, Bengtsson C, Lapidus L, et al.

J Endocrinol Invest. 1993 Feb; 16(2):129-31.

Smoking is associated with a spectrum of disorders. Recent reports have shown decreased serum concentrations of thyrotropin in euthyroid smokers, and there is an association between smoking and development of goiter (toxic and euthyroid). In a 12-year follow-up of a randomly selected sample of women we found a strong association between smoking at the time of initial screening and later development of hypothyroidism, the relative risk for a female smoker to develop hypothyroidism being 3.9 (95% confidence interval 1.6-9.1). There was, however, no association between smoking habits at the end of the follow-up and hypothyroidism. This indicates that several women who developed hypothyroidism may have done so in association with a change in smoking habits

Low selenium status in the elderly influences thyroid hormones.

Olivieri O, Girelli D, Azzini M, et al.

Clin Sci (Lond). 1995 Dec; 89(6):637-42.

1. Iodothyronine 5'-deiodinase, which is mainly responsible for peripheral triiodothyronine (T3) production, has recently been demonstrated to be a selenium-containing enzyme. In the elderly, reduced peripheral conversion of thyroxine (T4) to T3 and overt hypothyroidism are frequently observed. 2. We measured serum selenium and erythrocyte glutathione peroxidase (as indices of selenium status), thyroid hormones and thyroid-stimulating hormone in 109 healthy euthyroid subjects (52 women, 57 men), carefully selected to exclude abnormally low thyroid hormone levels induced by acute or chronic diseases or calorie restriction. The subjects were subdivided into three age groups. To avoid conditions of under-nutrition or malnutrition, dietary records were obtained for a sample of 24 subjects, randomly selected and representative of the whole population for age and sex. 3. In order to properly assess the influence of selenium status on iodothyronine 5'-deiodinase type I activity, a double-blind placebo-controlled trial was also carried out on 36 elderly subjects, resident at a privately owned nursing home. 4. In the free-living population, a progressive reduction of the T3/T4 ratio (due to increased T4 levels) and of selenium and erythrocyte glutathione peroxidase activity was observed with advancing age. A highly significant linear correlation between T4, T3/T4 and selenium was observed in the population as a whole (for T4, $R = -0.312$, $P < 0.002$; for T3/T4 ratio, $R = 0.32$, $P < 0.01$) and in older subjects (for T4, $R = -0.40$, $P < 0.05$; for T3/T4 ratio, $R = 0.54$, $P < 0.002$). 5. The main result of the double-blind placebo-controlled trial was a significant improvement of selenium indices and a decrease in the T4 level in selenium-treated subjects; serum selenium, erythrocyte glutathione peroxidase activity and thyroid hormones did not change in placebo-treated subjects. 6. We concluded that selenium status influences thyroid hormones in the elderly, mainly modulating T4 levels

Selenium deficiency and hypothyroidism: a new etiology in the differential diagnosis of hypothyroidism in children.

Pizzulli A, Ranjbar A.

Biol Trace Elem Res. 2000 Dec; 77(3):199-208.

Three female children presented with different clinical symptoms that could be related to impaired thyroid function. They underwent an accurate pediatric-endocrinologic diagnosis. Laboratory tests revealed no pathological findings, except latent hypothyroidism and selenium deficiency. Hypothyroidism was diagnosed by elevated basal TSH and by a pathological i.v.-TRH-stimulation test. After treating the children with sodium selenite orally for 4 wk, their metabolism had returned to normal and we saw a marked improvement of all clinical symptoms. For the first time, we have been able to describe hypothyroidism caused exclusively by selenium deficiency, the pathophysiology of which may be expressed as a malfunction of human 5'-deiodinases

Thyroxine treatment in patients with symptoms of hypothyroidism but thyroid function tests within the reference range: randomised double blind placebo controlled crossover trial.

Pollock MA, Sturrock A, Marshall K, et al.

OBJECTIVES: To determine whether thyroxine treatment is effective in patients with symptoms of hypothyroidism but with thyroid function tests within the reference range, and to investigate the effect of thyroxine treatment on psychological and physical wellbeing in healthy participants. **DESIGN:** Randomised double blind placebo controlled crossover trial. **SETTING:** Outpatient clinic in a general hospital. **Participants:** 25 patients with symptoms of hypothyroidism who had thyroid function tests within the reference range, and 19 controls. **Methods:** Participants were given thyroxine 100 microgram or placebo to take once a day for 12 weeks. Washout period was six weeks. They were then given the other to take once a day for 12 weeks. All participants were assessed physiologically and psychologically at baseline and on completion of each phase. **MAIN OUTCOME MEASURES:** Thyroid function tests, measures of cognitive function and of psychological and physical wellbeing. **RESULTS:** 22 patients and 19 healthy controls completed the study. At baseline, patients' scores on 9 out of 15 psychological measures were impaired when compared with controls. Patients showed a significantly greater response to placebo than controls in 3 out of 15 psychological measures. Healthy participants had significantly lower scores for vitality when taking thyroxine compared to placebo (mean (SD) 60 (17) v 73 (16), $P < 0.01$). However, patients' scores from psychological tests when taking thyroxine were no different from those when taking placebo except for a poorer performance on one visual reproduction test when taking thyroxine. Serum concentrations of free thyroxine increased and those of thyroid stimulating hormone decreased in patients and controls while they were taking thyroxine, confirming compliance with treatment. Although serum concentrations of free triiodothyronine increased in patients and controls taking thyroxine, the difference between the response to placebo and to thyroxine was significant only in the controls. **CONCLUSIONS:** Thyroxine was no more effective than placebo in improving cognitive function and psychological wellbeing in patients with symptoms of hypothyroidism but thyroid function tests within the reference range. Thyroxine did not improve cognitive function and psychological wellbeing in healthy participants

Are autoimmune thyroid dysfunction and depression related?

Pop VJ, Maartens LH, Leusink G, et al.

J Clin Endocrinol Metab. 1998 Sep; 83(9):3194-7.

The objective of this study was to examine the relationship between autoimmune thyroid disease and depression in perimenopausal women. Thyroid function [TSH, free T4, and thyroid peroxidase antibodies (TPO-Ab)] and depression (using the Edinburgh Depression Scale) were assessed cross-sectionally together with other determinants of depression. The subjects were 583 randomly selected perimenopausal women (aged 47-54 yr) from a community cohort of 6846 women. The main outcome measures were the occurrence of thyroid dysfunction (abnormal free T4 and/or TSH or elevated levels of TPO-Ab) and the concomitant presence of depression according to the Edinburgh Depression Scale. Neither biochemical thyroid dysfunction nor menopausal status was related to depression. Apart from several psycho-social determinants (the occurrence of a major life event, a previous episode of depression, or financial problems), an elevated level of TPO-Ab ($> \text{or} = 100 \text{ U/mL}$) was significantly associated with depression (odds ratio, 3.0, 95% confidence interval, 1.3-6.8). We conclude that women with elevated TPO-Ab levels are especially vulnerable to depression, whereas postmenopausal status does not increase the risk of depression

Hyperhomocysteinemia and low pyridoxal phosphate. Common and independent reversible risk factors for coronary artery disease.

Robinson K, Mayer EL, Miller DP, et al.

Circulation. 1995 Nov 15; 92(10):2825-30.

BACKGROUND: High plasma homocysteine is associated with premature coronary artery disease in men, but the threshold concentration defining this risk and its importance in women and the elderly are unknown. Furthermore, although low B vitamin status increases homocysteine, the link between these vitamins and coronary disease is unclear. **METHODS AND RESULTS:** We compared 304 patients with coronary disease with 231 control subjects. Risk factors and concentrations of plasma homocysteine, folate, vitamin B12, and pyridoxal 5'-phosphate were documented. A homocysteine concentration of $14 \text{ } \mu\text{mol/L}$ conferred an odds ratio of coronary disease of 4.8 ($P < .001$), and $5\text{-}\mu\text{mol/L}$ increments across the range of homocysteine conferred an odds ratio of 2.4 ($P < .001$). Odds ratios of 3.5 in women and of 2.9 in those 65 years or older were seen ($P < .05$). Homocysteine correlated negatively with all vitamins. Low pyridoxal 5'-phosphate ($< 20 \text{ nmol/L}$) was seen in 10% of patients but in only 2% of control subjects ($P < .01$), yielding an odds ratio of coronary disease adjusted for all risk factors, including high homocysteine, of 4.3 ($P < .05$). **CONCLUSIONS:** Within the range currently considered to be normal, the risk for coronary disease rises with increasing plasma homocysteine regardless of age and sex, with no threshold effect. In addition to a link with homocysteine, low pyridoxal-5'-phosphate confers an independent risk for coronary artery disease

Thyroid disorders and breast cancer.

Shering SG, Zbar AP, Moriarty M, et al.

We have investigated the controversial association between diseases of the thyroid gland and breast carcinoma using methodology which allows positive exclusion of cases of breast disease from control groups and the detection of subclinical alterations in thyroid volume using high resolution ultrasonography, thus addressing the deficiencies of earlier studies. Whereas the prevalence of hyperthyroidism and hypothyroidism in patients with breast carcinoma and in healthy controls without clinical evidence of breast disease was similar, non-toxic goitre was more than twice as common in the breast carcinoma patients. Thyroid volumes were also significantly higher in breast carcinoma patients than in controls; using World Health Organisation criteria, 45.5% of breast carcinoma patients had thyroid enlargement compared with only 10.5% of controls. Finally, antithyroid peroxidase autoantibodies were twice as common in breast cancer patients than in controls. These findings provide clear evidence of a relationship between thyroid disease and breast carcinoma, although the mechanisms underlying this relationship require further study, future studies of breast cancer risk factors should therefore include assessment of thyroid function, antibody status and volume

The thyroid and breast cancer: a significant association?

Smyth PP.

Ann Med. 1997 Jun; 29(3):189-91.

The coincidence of thyroid disorders and breast cancer has long been a subject of debate. Associations with hyperthyroidism, hypothyroidism, thyroiditis and nontoxic goitre have been reported. Although no convincing evidence exists of a causal role for overt thyroid disease in breast cancer, the preponderance of published work favours an association with hypothyroidism. Geographical variations in the incidence of breast cancer have been attributed to differences in dietary iodine intake and an effect of iodide on the breast has been postulated. Recent reports have shown a direct association between thyroid enlargement, as assessed by ultrasound, and breast cancer. Although the exact mechanism for the demonstrated association between diseases of the thyroid and breast cancer remains to be elucidated, there is at least the possibility that the presence of thyroid abnormalities may influence breast cancer progression and this alone should stimulate awareness into the coincidence of the two disorders

Daily migraine with visual aura associated with an occipital arteriovenous malformation.

Spierings EL.

Headache. 2001 Feb; 41(2):193-7.

A 51-year-old woman with daily attacks of migraine with visual aura is described. The aura always occurred on the right and the headache always on the left side of the head, suggesting a structural lesion in the left occipital lobe. The lesion appeared to be an arteriovenous malformation of which almost full obliteration resulted in a decrease in frequency of the aura and in intensity of the headache. Subsequent treatment of borderline hypothyroidism with levothyroxine brought about a dramatic improvement in frequency of both the aura and the headache. The case is discussed in the light of our present understanding of the pathogenesis of the migraine attack

[Levels of thyroid hormones and thyrotropic hormone in serum of women with perimenopausal arterial hypertension].

Stanosz S.

Ginekol Pol. 1992; 63(3):130-3.

Test carried out in 96 women aged between 43 to 55 years (50.46 +/- 4.7), who did not take any drugs during the last 3 months. The women were divided into two groups: premenopausal and early postmenopausal. Each group was subdivided according to blood pressure: with normal pressure and with arterial hypertension. The concentration of T4, T3 and TSH were measured using a radioimmunologic method. The saturation of carrier proteins was established with the T3/test, the result of which was used to divide T4 and T3 and to obtain FT4I and FT3I respectively. It was found that women with arterial hypertension have significantly higher ($p < 0.001$) TSH concentration. The concentration T3 and FT3I were significantly higher ($p < 0.01$) in women with arterial hypertension in the postmenopausal period

Serum dehydroepiandrosterone, dehydroepiandrosterone sulfate, and pregnenolone sulfate concentrations in patients with hyperthyroidism and hypothyroidism.

Clin Chem. 2000 Apr; 46(4):523-8.

BACKGROUND: Dehydroepiandrosterone (DHEA) and dehydroepiandrosterone sulfate (DHEA-S) have been suggested to have protective effects against cardiovascular disease, cancer, immune-modulated diseases, and aging. We examined serum concentrations of DHEA, DHEA-S, and pregnenolone sulfate (PREG-S) in patients with thyroid dysfunction. **METHODS:** Steroids extracted with methanol from serum sample were separated into an unconjugated fraction (DHEA) and a monosulfate fraction (DHEA-S and PREG-S), using a solid-phase extraction and an ion-exchange column. After separation of unconjugated steroids by HPLC, the DHEA concentration was measured by enzyme immunoassay. The monosulfate fraction was treated with arylsulfatase, and the freed steroids were separated by HPLC. The DHEA and PREG fractions were determined by gas chromatography-mass spectrometry, and the concentrations were converted into those of DHEA-S and PREG-S. **RESULTS:** Serum concentrations of DHEA, DHEA-S, and PREG-S were all significantly lower in patients with hypothyroidism (n = 24) than in age- and sex-matched healthy controls (n = 43). By contrast, in patients with hyperthyroidism (n = 22), serum DHEA-S and PREG-S concentrations were significantly higher, but the serum DHEA concentration was within the reference interval. Serum concentrations of these three steroids correlated with serum concentrations of thyroid hormones in these patients. Serum albumin and sex hormone-binding globulin concentrations were not related to these changes in the concentration of steroids. **CONCLUSIONS:** Serum concentrations of DHEA, DHEA-S, and PREG-S were decreased in hypothyroidism, whereas serum DHEA-S and PREG-S concentrations were increased but DHEA was normal in hyperthyroidism. Thyroid hormone may stimulate the synthesis of these steroids, and DHEA sulfotransferase might be increased in hyperthyroidism

Thyroid hormone replacement--one hormone or two?

Toft AD.

N Engl J Med. 1999 Feb 11; 340(6):469-70.

[Assessment of thyroid gland function in unwanted infertility--indications for TRH test and clinical impact from the viewpoint of the endocrinologist].

Vierhapper H.

Acta Med Austriaca. 1997; 24(4):133-5.

Disorders of thyroid function may cause infertility in women. Substitution with thyroxine will facilitate conception not only in women with manifest hypothyroidism, but also in patients with subclinical hypothyroidism. Thus, any screening program in female infertility should include a TRH-test

What is the optimal treatment for hypothyroidism?

Walsh JP, Stuckey BG.

Med J Aust. 2001 Feb 5; 174(3):141-3.

Standard treatment of primary hypothyroidism is with thyroxine, with the aim of relieving symptoms and bringing the serum TSH (thyroid-stimulating hormone) concentration to within the reference range. Recent research suggests that in some patients symptoms of hypothyroidism persist despite standard thyroxine replacement therapy. The optimal treatment of these patients is not known. Adjusting the thyroxine dose until the serum TSH concentration is in the lower part of the reference range (eg, 0.3-2.0 mU/L) may be beneficial. Animal studies and a single small clinical trial suggest that a combination of thyroxine and T3 (triiodothyronine), rather than thyroxine alone, may be required for optimal thyroid replacement therapy. Further research is needed to determine why some patients appear to have a suboptimal response to thyroxine, and whether combined thyroxine/T3 treatment is preferable to thyroxine alone in these patients

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