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Serum TSH, T_4, and Thyroid Antibodies in the United States Population (1988 to 1994): National Health and Nutrition Examination Survey (NHANES III)

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NHANES III measured serum TSH, total serum T_4, antithyroperoxidase (TPOAb), and antithyroglobulin (TgAb) antibodies from a sample of 17,353 people aged ≥12 yr representing the geographic and ethnic distribution of the U.S. population. These data provide a reference for other studies of these analytes in the U.S.

For the 16,533 people who did not report thyroid disease, goiter, or taking thyroid medications (disease-free population), we determined mean concentrations of TSH, T_4, TgAb, and TPOAb. A reference population of 13,344 people was selected from the disease-free population by excluding, in addition, those who were pregnant, taking androgens or estrogens, who had thyroid antibodies, or biochemical hypothyroidism or hyperthyroidism. The influence of demographics on TSH, T_4, and antibodies was examined.

Hypothyroidism was found in 4.6% of the U.S. population (0.3% clinical and 4.3% subclinical) and hyperthyroidism in 1.3% (0.5% clinical and 0.7% subclinical). (Subclinical hypothyroidism is used in this paper to mean mild hypothyroidism, the term now preferred by the American Thyroid Association for the laboratory findings described.) For the disease-free population, mean serum TSH was 1.50 (95% confidence interval, 1.46–1.54) mIU/liter, was higher in females than males, and higher in white non-Hispanics (whites) [1.57 (1.52–1.62) mIU/liter] than black non-Hispanics (blacks) [1.18 (1.14–1.21) mIU/liter] ($P < 0.001$) or Mexican Americans [1.43 (1.40–1.46) mIU/liter] ($P < 0.001$). TgAb were positive in 10.4 ± 0.5% and TPOAb, in 11.3 ± 0.4%; positive antibodies were more prevalent in women than men, increased with age, and TPOAb were less prevalent in blacks (4.5 ± 0.3%) than in whites (12.3 ± 0.5%) ($P < 0.001$). TPOAb were significantly associated with hypo or hyperthyroidism, but TgAb were not. Using the reference population, geometric mean TSH was 1.40 ± 0.02 mIU/liter and increased with age, and was significantly lower in blacks (1.18 ± 0.02 mIU/liter) than whites (1.45 ± 0.02 mIU/liter) ($P < 0.001$) and Mexican Americans (1.37 ± 0.02 mIU/liter) ($P < 0.001$). Arithmetic mean total T_4 was 112.3 ± 0.7 nmol/liter in the disease-free population and was consistently higher among Mexican Americans in all populations. In the reference population, mean total T_4 in Mexican Americans was (116.3 ± 0.7 nmol/liter), significantly higher than whites (110.0 ± 0.8 nmol/liter) or blacks (109.4 ± 0.8 nmol/liter) ($P < 0.0001$). The difference persisted in all age groups.

In summary, TSH and the prevalence of antithyroid antibodies are greater in females, increase with age, and are greater in whites and Mexican Americans than in blacks. TgAb alone in the absence of TPOAb is not significantly associated with thyroid disease. The lower prevalence of thyroid antibodies and lower TSH concentrations in blacks need more research to relate these findings to clinical status. A large proportion of the U.S. population unknowingly have laboratory evidence of thyroid disease, which supports the usefulness of screening for early detection. (*J Clin Endocrinol Metab* 87: 489–499, 2002)

IN THE TWENTIETH century, thyroid studies focused on goiter and iodine deficiency. Following the introduction of iodized salt and iodine in other foods, iodine deficiency was eliminated in the U.S. (1–4), and thyroid disease was related to other conditions, many of which are worsened by excessive iodine intake (5). NHANES III (1988–1994), and NHANES I (1971–1974) found that the median urinary iodine (UI) concentration decreased from 320 μg/liter to 145 μg/liter over the 20 yr (6). As part of a study of iodine nutrition in the U.S. from 1988–994, NHANES III also measured serum TSH, total serum T_4, and thyroid antibodies (TgAb, and TPOAb) in the U.S. Thyroid function tests in the U.S. previously have been limited to clinical settings or regions.

With the awareness that subclinical and clinical forms of hyperthyroidism and hypothyroidism in the U.S. are emerging as potential contributors to morbidity from osteoporosis, hyperlipidemia, hypercholesterolemia, hyperhomocysteinemia, and cardiovascular and neuropsychiatric disease, especially in the older population (7–11), we undertook the present study to provide reference data for TSH, T_4, TgAb, and TPOAb in the U.S. and evaluate the status of thyroid function from data using the population sampling methodology of NHANES III.

Abbreviations: I/Cr, Iodine/g creatinine; TgAb, antithyroglobulin; TPOAb, antithyroperoxidase; UI, urinary iodine.

Patients and Methods

Sample design

The NHANES surveys were designed to give national normative estimates of the health and nutritional status of the U.S. civilian, noninstitutionalized population. NHANES III was conducted from 1988 through 1994 using a stratified, multistage probability design. Young children, older people, blacks, and Mexican Americans were over-

TABLE 1. Prevalence and estimated numbers with hyperthyroidism and hypothyroidism, United States, by thyroid status and ethnicity: NHANES III (1988–1994)

	Hypothyroidism[a]						Hyperthyroidism[b]					
	Total		Clinical		Subclinical		Total		Clinical		Subclinical	
	No.[c]	%	No.	%	No.	%	No.	%	No.	%	No.	%
Total population												
All	9,597,742	4.6	688,140	0.3	8,909,602	4.3	2,610,097	1.3	1,102,763	0.5	1,507,334	0.7
White, non-Hispanic	8,049,845	5.1	607,921	0.4	7,441,924	4.8	2,170,749	1.4	901,521	0.6	1,269,228	0.8
Black, non-Hispanic	378,202	1.7	24,955	0.1	353,247	1.6	244,448	1.1	101,557	0.5	142,891	0.6
Mexican American	469,769	4.1	25,840	0.2	443,929	3.9	555,916	0.7	25,263	0.2	530,653	0.5
Remaining races	699,923	4.2	29,422	0.2	670,501	4.0	116,585	0.7	74,422	0.4	42,163	0.3
Total population—not pregnant and not taking estrogen												
All	8,551,415	4.5	649,919	0.3	7,901,496	4.2	2,355,038	1.2	899,858	0.5	1,455,180	0.8
White, non-Hispanic	7,098,903	5.1	574,396	0.4	6,524,507	4.7	1,959,403	1.4	725,210	0.5	1,234,193	0.9
Black, non-Hispanic	359,012	1.7	20,260	0.1	338,752	1.6	218,855	1.0	82,891	0.4	135,964	0.6
Mexican American	450,106	4.2	25,840	0.2	424,266	4.0	64,207	0.6	21,347	0.2	42,860	0.4
Remaining races	643,393	3.9	29,423	0.2	613,970	3.8	112,573	0.7	70,410	0.4	42,163	0.3
Population self-reporting thyroid disease, goiter, or taking thyroid medication												
All	1,562,378	15.0	224,779	2.2	1,337,599	12.8	1,907,233	18.3	766,267	7.3	1,140,966	10.9
White, non-Hispanic	1,326,816	14.5	197,039	2.1	1,129,777	12.3	1,743,885	18.9	678,240	7.3	1,065,645	11.5
Black, non-Hispanic	52,167	9.0	8,916	1.5	43,251	7.5	97,831	16.9	44,132	7.6	53,699	9.3
Mexican American	53,583	22.9	6,392	2.7	47,191	20.2	37,067	15.8	15,444	6.6	21,623	9.2
Remaining races	119,812	32.1	12,432	3.3	107,380	28.8	28,451	7.6	28,451	7.6	0	0.0
Disease-free population												
All	8,035,363	4.1	463,361	0.2	7,572,002	3.9	702,864	0.4	336,496	0.2	366,368	0.2
White, non-Hispanic	6,713,029	4.6	410,882	0.3	6,302,147	4.3	426,864	0.3	223,281	0.2	203,583	0.1
Black, non-Hispanic	326,036	1.5	16,040	0.1	309,996	1.4	146,617	0.7	57,425	0.3	89,192	0.4
Mexican American	416,186	3.8	19,448	0.2	396,738	3.6	41,248	0.4	9,818	0.1	31,430	0.3
Remaining races	580,113	3.5	16,991	0.1	563,122	3.4	88,134	0.5	45,971	0.3	42,163	0.3

[a] Clinical hypothyroidism: TSH >4.5 mU/liter and T_4 <57.9 nmol/liter; subclinical hypothyroidism: TSH >4.5 mU/liter and T_4 ≥57.9 nmol/liter.

[b] Clinical hyperthyroidism: TSH <0.1 mU/liter and T_4 ≥169.9 nmol/liter; subclinical hyperthyroidism: TSH <0.1 mU/liter and T_4 <169.9 nmol/liter.

[c] Number of people is the population estimated from the weights assigned to the representative individuals sampled and tested.

sampled to provide sufficient numbers for studies of those groups (12, 13). This study focuses on the 17,353 people aged ≥12 yr who had thyroid studies, representing the weighted population of 205,562,185 people. (In NHANES III, each person sampled is mathematically weighted to represent a specific number and proportion of people in the population and during analysis that weighting is used to adjust for any oversampling.) Thyroid hormone tests were done on a sample of people 12 yr of age or older. Serum was frozen (−20 C) and shipped on dry ice to the University of Southern California, Endocrine Services Laboratory (Los Angeles, CA) for analysis of thyroid antibodies and TSH (14). Serum T_4 was sent for analysis to the White Sands Research Center (Alamogorda, NM). Fasting urine specimens were collected, frozen (−20 C), and shipped on dry ice to the Iodine Research Laboratory, University of Massachusetts Medical Center (Worcester, MA) for UI and to the University of Minnesota Medical School for urinary creatinine (14).

Information was collected on age, sex, income levels, metropolitan/nonmetropolitan residency, and ethnicity. Ethnicity was categorized as white non-Hispanic (whites), black non-Hispanic (blacks), Mexican American, and remaining ethnic groups. A diagnosis of thyroid disease was made from historical information on goiter, thyroid diseases, and use of thyroid medication; however, there was no examination of the neck for goiter or thyroid size.

Laboratory methods

T_4. T_4 was measured using an immunoassay for T_4 (Roche Molecular Biochemicals, Indianapolis, IN), which had a reference (normal) range of 57.9 nmol/liter to 169.9 nmol/liter (4.5 μg/dl to 13.2 μg/dl).

TSH. TSH was measured with a chemiluminescence immunometric assay (Nichols Institute Diagnostics, San Juan Capistrano, CA) (15). The working range for this method is 0.01mIU/liter to 50 mIU/liter. The reference (normal) range for the test was 0.39–4.6 mIU/liter.

TgAb and TPOAb. TPOAb and TgAb were measured by a highly sensitive, direct RIA system (Kronus, San Clemente, CA) (16, 17). The normal range for TgAb in humans is <1.0 IU/ml, and for TPOAb, <0.5 IU/ml.

Iodine. UI concentrations were determined using the Sandell-Koltoff reaction (18, 19).

Creatinine. Urine creatinine was measured by the Jaffè alkaline picrate method, to adjust iodine concentration for creatinine concentration [μg iodine/g creatinine(I/Cr)] (14, 18).

Statistical analyses

We analyzed data with SUDAAN software (Research Triangle Institute, Triangle Park, NC) for the statistical analysis of correlated data (20) to account for the complex sample survey design using the weights assigned to the individuals sampled to represent the U.S. population.* *P* values and confidence intervals are large sample results calculated by SUDAAN and accounts for the survey design. (The individuals interviewed and examined were given weights to represent the composition of the total United States civilian, noninstitutionalized population. In our analysis, we further adjusted the population on which iodine or the thyroid related analytes were collected to reflect the composition of the U.S. population.)

Regions and race in NHANES III were standardized for age and sex using the distribution of the entire population.

The means and SEM for TSH were calculated from logarithmic transformed values; for T_4, arithmetic means with SEM. The median, 2.5 and 97.5 percentiles were calculated to generate possible reference limits for TSH and T_4 from the reference population (21, 22).

To study the characteristics of persons with high or low TSH and/or the presence of antibodies, we calculated prevalence, prevalence differences, prevalence ratios, and odds ratios. Logistic regression was used to determine the association of high or low TSH values with other variables including sex, age, ethnic group, poverty level, urban/rural status, region, presence of thyroid antibodies, and UI concentration. Effect modification was assessed by including interaction terms. For

these analyses, high TSH was defined as a concentration >4.5 mIU/liter and low TSH as a value <0.1 mIU/liter; high T_4 is a concentration ≥169.9 nmol/liter and low T_4, a concentration <57.9 nmol/liter. Hyperthyroidism was defined as clinically significant if TSH <0.1 mIU/liter and T_4 ≥169.9 nmol/liter and as subclinical or mild when TSH <0.1 mIU/liter and T_4 <169.9 nmol/liter. Hypothyroidism was defined as clinically significant if TSH >4.5 mIU/liter and T_4 <57.9 nmol/liter and as subclinical or mild when TSH >4.5 mIU/liter and T_4 ≥57.9 nmol/liter. We chose 0.1 mIU/liter for the lower normal value for TSH instead of the laboratory reference range of 0.39 mIU/liter because values between 0.1 mIU/liter and 0.39 mIU/liter are generally considered clinically insignificant using this sensitive TSH assay.

Linear regression analysis was used to assess the association of TSH, after logarithmic transformation, with other characteristics. We screened for potential colinearity by assessing the correlations between independent variables.

Results

We studied the 17,353 people ≥ age 12 yr for whom TSH, T_4, and thyroid antibodies were available (the total population), 4.6% of whom had hypothyroidism [an estimated 9,597,742 people in the U.S. (0.3% clinical and 4.3% subclinical], and 1.3% had hyperthyroidism [an estimated 2,610,097 people (0.5% clinical and 0.7% subclinical)]. Because free T_4 was not available and because estrogen influences total T_4 concentrations, we reanalyzed the total population for thyroid disease after excluding individuals who were pregnant or taking estrogen (Table 1.). There were significantly more females than males with combined subclinical and clinical hypothyroidism in the age groups 50–59 yr and 60–69 yr ($P < 0.01$). Of the 820 people in the total population who self reported thyroid disease or who were taking thyroid medications, 15.0% had biochemical evidence of hypothyroidism (2.2% clinical, 12.8% subclinical), and 18.3% had hyperthyroidism (7.3% clinical, 10.9% subclinical). This finding supports the usefulness of self reporting of thyroid disease in NHANES III but suggests that only 67% of those with thyroid disease may have been appropriately treated. This survey estimates that 10.4 million people in the U.S. had thyroid disease, goiter, or were taking thyroid medication (estimated from the sample who self-reported). For those not reporting thyroid disease, an estimated additional 8.7 million people, showed biochemical evidence of either hypothyroidism or hyperthyroidism, 9.2% of them with clinically significant thyroid disease (Table 1).

We separated the 820 people who self-reported thyroid disease, goiter, or who were taking thyroid medications from the total population leaving a sample of 16,533 people who represented an disease-free population estimated to be 195,134,687 people. A reference population was then created from the disease-free population by excluding people who had recognized risk factors for thyroid function, namely people who were pregnant, taking estrogens, androgens, or lithium, or who had detectable TgAb, TPOAb, or laboratory evidence of hyperthyroidism or hypothyroidism (21). The reference population (13,344 in the sample) represented a population estimated to be 152,047,466 people (Table 2).

Population distribution of individual thyroid analytes

TSH. The geometric mean serum TSH for the total population was 1.47 (95% confidence interval 1.44–1.51) mIU/liter. It

TABLE 2. The U.S. populations age 12 yr and older with measured TSH, T_4, AbTg, and AbTPO, by factors affecting thyroid function: 1988–1994 (NHANES III)

	All				Males				Females			
	Sample		Population		Sample		Population		Sample		Population	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Total Population[a]												
All	17,353	100.0	205,562,185	100.0	8,043	46.3	98,780,190	48.1	9,310	53.7	106,781,995	51.9
White, non-Hispanic	6,850	39.5	154,964,259	75.4	3,148	18.1	74,944,956	36.5	3,702	21.3	80,019,302	38.9
Black, non-Hispanic	4,895	28.2	22,508,076	10.9	2,198	12.7	10,110,219	4.9	2,697	15.5	12,397,856	6.0
Mexican American	4,864	28.0	11,254,385	5.5	2,382	13.7	5,807,746	2.8	2,482	14.3	5,446,639	2.6
Remaining races	744	4.3	16,835,466	8.2	315	1.8	7,917,269	3.9	429	2.5	8,918,197	4.3
Population reporting thyroid disease, goiter, or taking thyroid medication												
All	820	100.0	10,427,498	100.0	129	15.7	1,640,840	15.7	691	84.3	8,786,659	84.3
White, non-Hispanic	524	63.9	9,242,039	88.6	81	9.9	1,478,074	14.2	443	54.0	7,763,965	74.5
Black, non-Hispanic	139	17.0	578,628	5.5	21	2.6	70,799	0.7	118	14.4	507,829	4.9
Mexican American	135	16.5	234,145	2.2	23	2.8	43,128	0.4	112	13.7	191,017	1.8
Remaining races	22	2.7	372,685	3.6	4	0.5	48,838	0.5	18	2.2	323,848	3.1
Disease-free population[b]												
All	16,533	100.0	195,134,687	100.0	7,914	47.9	97,139,351	49.8	8,619	52.1	97,995,336	50.2
White, non-Hispanic	6,326	38.3	145,722,219	74.7	3,067	18.6	73,466,882	37.6	3,259	19.7	72,255,337	37.0
Black, non-Hispanic	4,756	28.8	21,929,447	11.2	2,177	13.2	10,039,420	5.1	2,579	15.6	11,890,028	6.1
Mexican American	4,729	28.6	11,020,240	5.6	2,359	14.3	5,764,618	3.0	2,370	14.3	5,255,622	2.7
Remaining races	722	4.4	16,462,780	8.4	311	1.9	7,868,431	4.0	411	2.5	8,594,349	4.4
Reference population[c] (disease-free without risk factors[b])												
All	13,344	100.0	152,047,466	100.0	7,162	53.7	86,297,010	56.8	6,182	46.3	65,750,456	43.2
White, non-Hispanic	4,689	35.1	110,189,488	72.5	2,644	19.8	64,137,706	42.2	2,045	15.3	46,051,782	30.3
Black, non-Hispanic	4,212	31.6	19,400,724	12.8	2,085	15.6	9,650,120	6.3	2,127	15.9	9,750,605	6.4
Mexican American	3,864	29.0	9,116,405	6.0	2,151	16.1	5,310,574	3.5	1,713	12.8	3,805,832	2.5
Remaining races	579	4.3	13,340,848	8.8	282	2.1	7,198,611	4.7	297	2.2	6,142,237	4.0

[a] Population with TSH, T_4, TgAb, and TPOAb measured (including those with thyroid disease, goiter, medications, and risk factors[c]).
[b] Disease-free population has excluded people who reported thyroid disease, goiter, or taking thyroid medication.
[c] Reference population is the disease-free population without the risk factors of pregnancy, taking estrogen, androgen, or lithium no detectable thyroid antibodies, and without laboratory evidence of hypothyroidism or hyperthyroidism.

TABLE 3. Comparison of TSH concentrations by population gender and ethnicity, United States; NHANES III (1988–1994)

	Mean serum TSH (mU/liter)						% Serum TSH >4.5 mU/liter						% Serum TSH <0.4 mU/liter					
	Total		Males		Females		Total		Males		Females		Total		Males		Females	
	Mean	SE	Mean	SE	Mean	SE	%	SE	%	SE	%	SE	%	SE	%	SE	%	SE
Total Population																		
All	1.47	0.02	1.46	0.02	1.49	0.02	4.7	0.3	3.4	0.3	5.8	0.4	3.2	0.2	1.8	0.2	4.4	0.4
White, non-Hispanic	1.53	0.02	1.51	0.02	1.55	0.03	5.2	0.3	3.7	0.3	6.6	0.5	3.0	0.3	1.6	0.2	4.3	0.5
Black, non-Hispanic	1.17	0.02	1.20	0.03	1.15	0.02	1.7	0.2	1.9	0.4	1.5	0.2	4.6	0.4	3.6	0.5	5.3	0.6
Mexican Americans	1.43	0.03	1.43	0.03	1.43	0.04	4.2	0.4	2.4	0.4	6	0.7	2.6	0.2	1.8	0.3	3.5	0.3
Disease-free population[a]																		
All	1.50	0.02	1.47	0.02	1.57	0.02	4.1	0.3	3.1	0.3	5.1	0.4	1.8	0.2	1.4	0.2	2.3	0.3
White, non-Hispanic	1.57	0.02	1.52	0.02	1.62	0.03	4.6	0.4	3.4	0.3	5.8	0.5	1.4	0.2	1.1	0.2	1.7	0.3
Black, non-Hispanic	1.18	0.02	1.21	0.03	1.16	0.02	1.5	0.2	1.8	0.4	1.2	0.2	4.0	0.4	3.5	0.5	4.5	0.6
Mexican Americans	1.43	0.03	1.43	0.03	1.43	0.03	3.8	0.4	2.4	0.4	5.3	0.7	2.1	0.2	1.7	0.3	2.6	0.3
Population with risk factors[b]																		
All	1.71	0.05	1.84	0.09	1.67	0.06	12.9	0.8	14.3	1.7	12.4	0.9	7.4	0.5	6.2	0.9	7.8	0.7
White, non-Hispanic	1.75	0.05	1.93	0.12	1.70	0.06	13.5	0.8	15.1	1.9	13.0	1.0	7.4	0.6	5.8	1.0	7.9	0.8
Black, non-Hispanic	1.12	0.06	0.97	0.23	1.15	0.06	4.9	0.8	9.5	3.0	4.1	0.8	11.6	1.5	19.3	5.9	10.2	1.8
Mexican Americans	1.74	0.11	1.81	0.21	1.72	0.13	14.4	1.6	12.9	2.6	14.9	2.1	6.0	0.8	3.9	1.9	6.7	0.9
Reference population[c]																		
All	1.40	0.02	1.41	0.02	1.38	0.02	1.8	0.2	1.8	0.2	1.7	0.3	1.6	0.2	1.2	0.2	2.2	0.4
White, non-Hispanic	1.45	0.02	1.45	0.02	1.45	0.03	1.8	0.2	1.8	0.2	1.9	0.3	1.2	0.2	0.9	0.2	1.7	0.5
Black, non-Hispanic	1.18	0.02	1.22	0.02	1.14	0.02	1.2	0.2	1.6	0.4	0.8	0.2	3.4	0.4	2.9	0.4	4.0	0.5
Mexican Americans	1.39	0.02	1.40	0.02	1.32	0.02	1.8	0.3	1.5	0.3	2.2	0.5	1.8	0.2	1.6	0.3	2.1	0.4

[a] Disease-free population excludes those reporting thyroid disease, goiter, or taking thyroid medication.
[b] Population with risk factors includes only those reporting thyroid disease, goiter, or taking thyroid medication and those who are pregnant, taking estrogen, androgen or lithium, or with measurable thyroid antibodies.
[c] Reference population is the disease free population excluding those who are pregnant, taking estrogen, androgen or lithium, or with measurable thyroid antibodies or chemical evidence of hypothyroidism or hyperthyroidism.

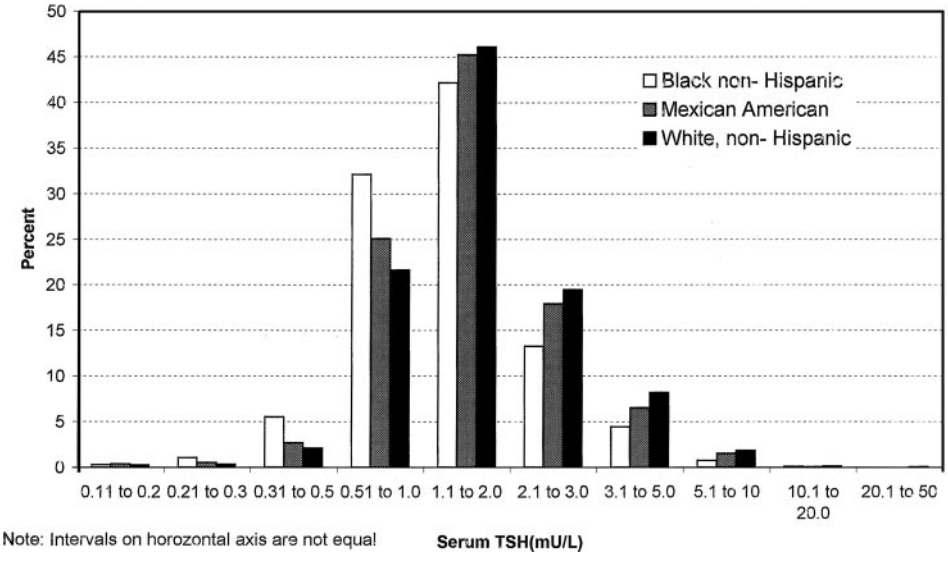

FIG. 1. Serum TSH distribution in U.S. reference population by ethnicity. (Population without thyroid disease, goiter, or taking thyroid medication and without risk factors that include pregnancy, taking estrogen, androgens, or lithium, and the presence of thyroid antibodies and biochemical evidence of hypothyroidism or hyperthyroidism.) The shift to the left among blacks is significantly different from whites and Mexican Americans ($P < 0.001$). There was no significant difference in the distribution between whites and Mexican Americans.

was higher in the disease-free population [1.50 (1.46–1.54) mIU/liter] but was lower in the reference population [1.40 (1.37–1.44) mIU/liter]. Mean TSH concentration and the percent with TSH >4.5mIU/liter was significantly higher in females than males in the total population ($P < 0.01$), and the disease-free population ($P < 0.05$) but not in the reference population (Table 3).

The percentage of people with TSH <0.4 was significantly higher in females than males in the three population groupings ($P < 0.05$). Blacks had significantly lower mean TSH concentrations than whites in all populations ($P < 0.01$). The percent of blacks with TSH >4.5 mIU/liter was significantly lower than whites in the total and disease-free population ($P < 0.001$) but not in the reference population. The percent with TSH <0.4 mIU/liter was significantly higher in blacks than whites ($P < 0.01$) in the three defined populations (Table 3).

In the reference population, the TSH concentration distribution of blacks was shifted to the left compared with whites and Mexican Americans even within the normal range (Fig. 1). People with risk factors had significantly higher mean TSH concentrations than those in the reference population, *i.e.* without risk factors. We continued to find the increase in TSH concentration associated with age in men and women without risk factors, but the difference between males and

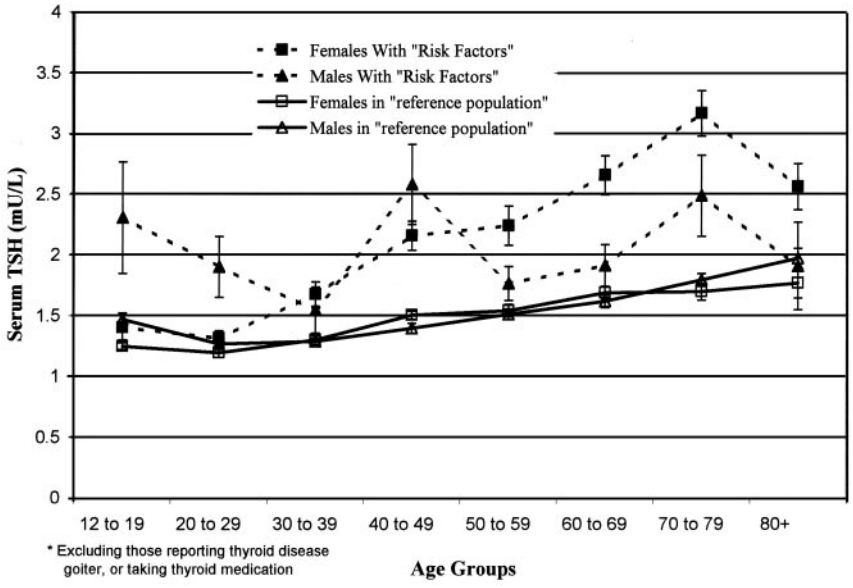

FIG. 2. Serum TSH in the disease-free population (excluding those self-reporting thyroid disease, goiter, or taking thyroid medication) with and without risk factors. (Risk factors include pregnancy, taking estrogen, androgens, or lithium, and the presence of thyroid antibodies and biochemical evidence of hypothyroidism or hyperthyroidism.) In the group of individuals with risk factors, females had significantly higher serum TSH than males in nearly every age group age 30 yr and above. One male in age group 40–49 yr had biochemical hypothyroidism with TSH in excess of 300 mIU/liter but did not report thyroid disease at the time of the interview. Below age 30 yr, males with risk factors had significantly higher TSH. In the reference population, the difference in male and female TSH concentration was not significant.

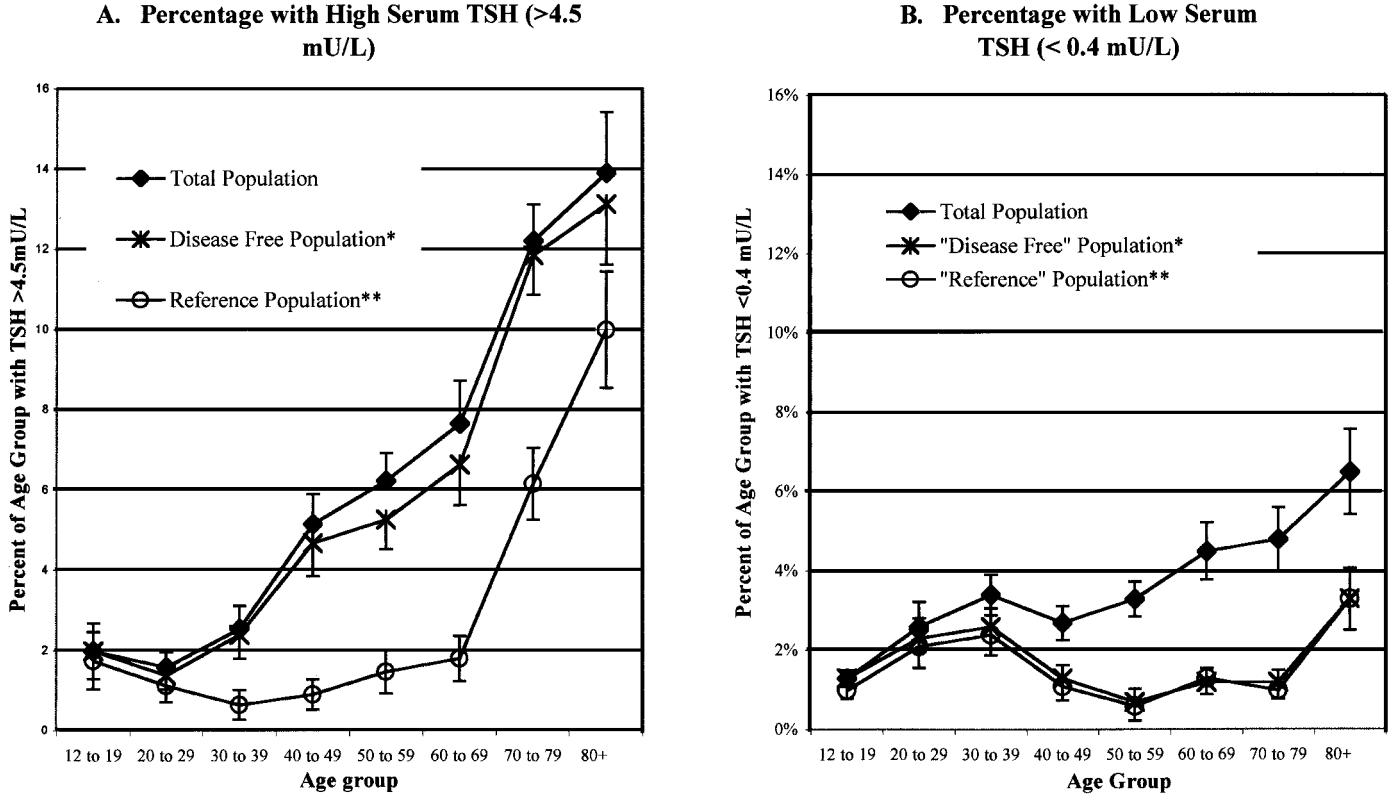

FIG. 3. Percentage with high or low serum TSH in the total U.S. population, the disease-free (excludes those people who have reported having thyroid disease, goiter, or taking thyroid medications) and reference population (excludes those people who reported having thyroid disease, goiter, or taking thyroid medications and do not have risk factors that include pregnancy, taking estrogen, androgens, or lithium, and are without the presence of thyroid antibodies or biochemical evidence of hypothyroidism or hyperthyroidism) by age. A, High serum TSH. In the disease-free population, the percentage of people with high serum TSH concentration (>4.5 mIU/liter) is slightly lower than that of the total population but significantly higher than the percentage in the reference population. B, Low serum TSH. The percentage of people with low serum TSH in the disease-free population, on the other hand, is significantly lower than the percentage in the total population and similar to the pattern seen in the reference population. Note the elevated prevalence of low TSH in the populations without thyroid disease or risk factors at ages 20–39 yr and again after age 79 yr. The higher prevalence of individuals with low TSH or high TSH in the total population is related directly to the people reporting thyroid disease, goiter, or taking thyroid medication and probably reflects inadequate management of clinical thyroid disease.

females was smaller when risk factors were absent (Fig. 2). The difference in mean TSH concentrations was also significant between whites with and without risk factors and between Mexican Americans with and without risk factors but was not significant between blacks with or without risk factors (Fig. 4).

The slight difference in the percent with TSH >4.5 mIU/liter when comparing total and disease-free populations persisted in all age groups (Fig. 3A). Elevated serum TSH values were more frequent in females than in males in age groups 40–49 ($P < 0.05$), 50–59 ($P < 0.01$), and 60–69 ($P < 0.001$). The prevalence pattern by age of people with TSH <0.4 mIU/liter was similar in the disease-free and reference population and quite different from people in the total population (Fig. 3B). The higher prevalence of low TSH in the total population was due to the abnormal laboratory values among people who self-reported thyroid disease, goiter, and taking thyroid medication, perhaps reflecting inappropriate treatment of the underlying disease.

The TSH median and 2.5 and 97.5 percentiles were calculated for the total population, the disease-free population, and the reference population (Table 4). Estimated from the reference population, the median TSH concentration was 1.39 (1.35–1.47) mIU/liter with the 95% TSH reference limits between 0.45 (0.42–0. 47) mIU/liter and 4.12 (3.94–4.45) mIU/liter. The median TSH concentration increased with age after age 20 yr in all populations, even in the reference population where thyroid antibodies and other risk factors were excluded.

T_4

For the disease-free population, the mean total T_4 was 112.3 ± 0.7 nmol/liter (8.7 ± 0.1 μg/dl) After age 20 yr, T_4 concentrations decreased significantly with age ($P < 0.001$). In the reference population, total T_4 in Mexican Americans (116.3 ± 0.7 nmol/liter) was significantly higher than whites (110.0 ± 0.8 nmol/liter) or blacks (109.4 ± 0.8 nmol/liter) ($P < 0.0001$). The difference persisted in all age groups and in the disease-free population as well. There was no significant difference in the T_4 concentrations between whites and blacks.

In the reference population, the median T_4 concentration was 109.3 (107.3–111.8) nmol/liter [8.5 (8.3–8.7) μg/dl] with the 95% reference limits between 65.2 (64.3–66.8) nmol/liter and 162.8 (155.8–165.8) nmol/liter (5.1 and 12.6 μg/dl) (Table 5).

Thyroid antibodies

In the total population, positive TPOAb (≥0.5 IU/ml) were detected in 13.0 ± 0.4%, and positive TgAb (≥1.0 IU/ml) was detected in 11.5 ± 0.5%. The prevalence of positive antibodies was lower in the disease-free population: TPOAb, 11.3 ± 0.4% and TgAb, 10.4 ± 0.5%. The prevalence of positive

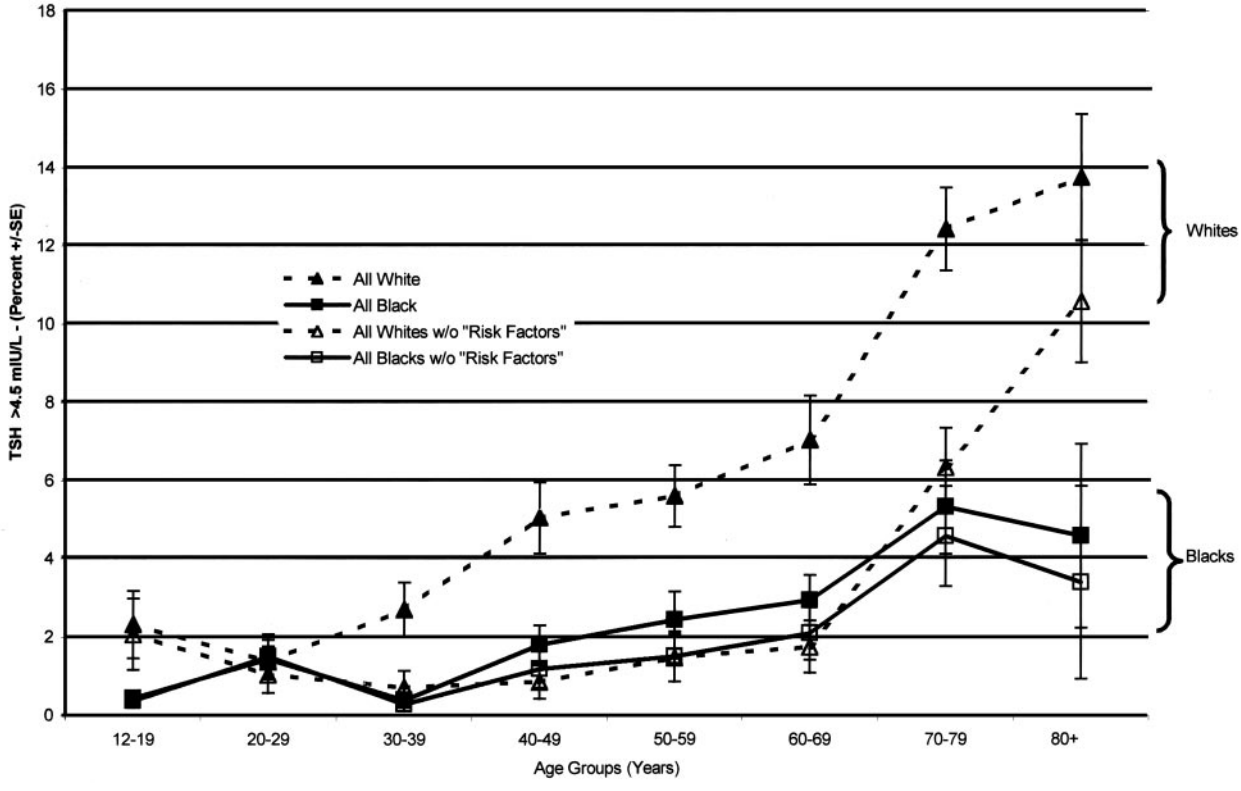

FIG. 4. Comparison of the effect of risk factors on high serum TSH (>4.5 mIU/liter) in blacks and whites. When comparing high TSH concentration in the disease-free population (excludes those people who have reported having thyroid disease, goiter, or taking thyroid medications) with the reference population (excludes those people who reported having thyroid disease, goiter, or taking thyroid medications and who do not have risk factors that include pregnancy, taking estrogen, androgens, or lithium, and are without the presence of thyroid antibodies or biochemical evidence of hypothyroidism or hyperthyroidism), the significant effect of risk factors in whites is not seen in blacks. In the reference population, the prevalence of high TSH in whites does not increase until age 70 yr.

TABLE 4. Serum TSH concentration[a] (median, 2.5 and 97.5 centiles) by population characteristics, age, gender and ethnicity, United States; NHANES III (1988–1994)

Ethnicity	Centile	Total population			Disease-free population[b]			Reference population (risk factors[c] excluded)		
		Total	Male	Female	Total	Male	Female	Total	Male	Female
Total	2.5	0.33	0.44	0.21	0.44	0.46	0.41	0.45	0.47	0.41
	Median	**1.49**	**1.48**	**1.49**	**1.49**	**1.48**	**1.50**	**1.39**	**1.40**	**1.37**
	97.5	5.8	5.1	7.12	5.52	4.81	6.10	4.12	4.15	4.09
Whites	2.5	0.33	0.46	0.14	0.48	0.49	0.47	0.49	0.50	0.46
	Median	**1.5**	**1.5**	**1.58**	**1.50**	**1.50**	**1.58**	**1.43**	**1.47**	**1.41**
	97.5	6.47	5.35	7.84	5.73	5.00	6.77	4.18	4.16	4.19
Blacks	2.5	0.29	0.35	0.26	0.32	0.35	0.30	0.35	0.37	0.32
	Median	**1.19**	**1.22**	**1.17**	**1.19**	**1.22**	**1.17**	**1.19**	**1.22**	**1.17**
	97.5	3.9	4	3.85	3.81	3.89	3.69	3.63	3.82	3.35
Mexican Americans	2.5	0.37	0.44	0.33	0.41	0.45	0.38	0.43	0.45	0.40
	Median	**1.4**	**1.41**	**1.40**	**1.40**	**1.41**	**1.39**	**1.36**	**1.40**	**1.30**
	97.5	5.72	4.32	6.65	5.30	4.32	6.31	3.91	3.80	4.34
Remaining races	2.5	0.38	0.43	0.36	0.39	0.43	0.37	0.40	0.44	0.38
	Median	**1.45**	**1.39**	**1.49**	**1.41**	**1.38**	**1.49**	**1.36**	**1.39**	**1.32**
	97.5	5.01	4.87	5.19	4.83	4.83	4.84	4.19	4.85	4.04
Age: all ethnic groups										
12–19	2.5	0.45	0.48	0.41	0.44	0.48	0.40	0.46	0.48	0.44
	Median	**1.37**	**1.5**	**1.25**	**1.37**	**1.50**	**1.25**	**1.35**	**1.50**	**1.20**
	97.5	4.2	4.64	3.66	4.20	4.64	3.65	4.07	4.60	3.59
20–29	2.5	0.38	0.45	0.36	0.39	0.45	0.38	0.40	0.46	0.38
	Median	**1.28**	**1.3**	**1.26**	**1.28**	**1.30**	**1.26**	**1.26**	**1.28**	**1.18**
	97.5	4.07	4.13	3.99	4.02	4.09	3.88	3.56	3.56	3.52
30–39	2.5	0.34	0.46	0.28	0.41	0.46	0.33	0.42	0.49	0.32
	Median	**1.35**	**1.3**	**1.40**	**1.35**	**1.30**	**1.41**	**1.29**	**1.28**	**1.34**
	97.5	4.85	4.3	5.32	4.57	4.25	4.71	3.69	3.67	3.70
40–49	2.5	0.37	0.39	0.33	0.49	0.42	0.60	0.50	0.44	0.60
	Median	**1.5**	**1.43**	**1.59**	**1.50**	**1.43**	**1.59**	**1.40**	**1.38**	**1.48**
	97.5	6.56	6.2	6.58	5.75	5.25	5.77	3.82	3.77	3.92
50–59	2.5	0.31	0.49	0.06	0.52	0.53	0.52	0.52	0.50	0.53
	Median	**1.6**	**1.58**	**1.69**	**1.60**	**1.58**	**1.70**	**1.50**	**1.51**	**1.49**
	97.5	7.58	4.62	11.60	5.73	4.47	10.74	4.03	4.04	4.02
60–69	2.5	0.13	0.36	0.03	0.48	0.55	0.45	0.49	0.56	0.45
	Median	**1.78**	**1.67**	**1.98**	**1.79**	**1.67**	**1.99**	**1.67**	**1.66**	**1.68**
	97.5	9.87	5.64	11.96	7.48	4.89	11.64	4.33	4.27	4.48
70–79	2.5	0.04	0.37	0.02	0.46	0.45	0.46	0.45	0.47	0.44
	Median	**1.91**	**1.87**	**1.99**	**1.98**	**1.88**	**2.00**	**1.76**	**1.79**	**1.69**
	97.5	9.86	9.68	12.04	9.80	8.72	12.97	5.90	6.39	5.77
80+	2.5	0.04	0.31	0.03	0.33	0.33	0.30	0.33	0.36	0.17
	Median	**1.99**	**1.98**	**2.00**	**2.08**	**1.99**	**2.10**	**1.90**	**1.97**	**1.81**
	97.5	12.26	8.26	12.85	9.36	7.75	10.79	7.50	6.82	7.87

[a] TSH = mIU/liter.
[b] Population excluding people who reported thyroid disease, goiter, or taking thyroid medication.
[c] Risk factors, pregnancy, estrogens, androgens, lithium, antithyroid antibodies, chemical hypothyroidism, and chemical hyperthyroidism.

TPOAb and positive TgAb in the total and disease-free population was higher in females than males ($P < 0.001$) and increased with age, especially among females. The percentage of whites with positive TPOAb and TgAb was higher than the percentage of blacks ($P < 0.001$) or Mexican Americans ($P < 0.01$) (Table 6).

Approximately 18% of the disease-free population had detectable TgAb or TPOAb Of those with positive TgAb, 69.9% also had positive TPOAb; and of those with positive TPOAb, 54.5% also had positive TgAb. TPOAb was positive alone in 4.4%, and TgAb was positive alone in 3.4%. TPOAb and TgAb were detected together in 6.9%.

Interrelationships of analytes

Using linear regression, concentrations of TSH in the total population were associated with positive TPOAb concentrations ($P < 0.01$) but not with positive TgAb concentrations ($P = 0.6$), when both were included in the model.

Using logistic regression, the prevalence of TSH values >4.5 mIU/liter was associated with the presence of positive TPOAb (OR = 8.4, 5.8–12.1) ($P < 0.0001$) and less strongly associated with positive TgAb (OR = 1.8, 1.3–2.7) ($P < 0.01$). The significant association between female gender and elevated TSH disappeared after controlling for positive TPOAb. The prevalence of clinical hypothyroidism was strongly associated with positive TPOAb (OR = 39.7, 11.6–136.1) ($P < 0.0001$) but was not associated with positive TgAb ($P = 0.3$). No individual with hypothyroidism had positive TgAb in the absence of positive TPOAb. The prevalence of TSH <0.4 was associated with positive TPOAb (OR = 3.0, 2.1–4.2) ($P < 0.0001$) but not TgAb ($P = 0.85$). The prevalence of clinical hyperthyroidism was associated with positive TPOAb (OR =

TABLE 5. Serum total thyroxine concentration[a] (median, 2.5 and 97.5 centiles) by population characteristics, gender, and ethnicity, United States; NHANES III (1988–1994)

Percentile	Total population			Disease-fFree population[b]			Reference population[c]		
	Total	Male	Female	Total	Male	Female	Total	Male	Female
Total									
2.5	62.9	63.1	62.8	63.6	63.2	63.9	65.2	64.4	66.9
Median	**110.6**	**106.9**	**114.1**	**110.3**	**106.8**	**113.7**	**109.3**	**107.3**	**111.8**
97.5	171.7	156.6	180.7	168.2	156.1	175.8	162.8	156.0	165.9
Whites									
2.5	62.6	64.5	61.4	63.2	64.5	62.4	65.1	65.6	63.9
Median	**110.1**	**106.6**	**113.6**	**109.7**	**106.5**	**113.0**	**108.6**	**107.0**	**110.5**
97.5	171.7	155.2	180.9	167.0	154.4	175.7	160.2	154.9	164.9
Blacks									
2.5	62.2	59.9	65.8	62.6	59.9	66.0	62.8	60.2	67.4
Median	**108.5**	**102.6**	**113.1**	**108.3**	**102.6**	**113.1**	**107.1**	**102.4**	**111.3**
97.5	172.3	160.3	179.3	170.4	159.3	176.5	162.8	154.1	168.1
Mexican Americans									
2.5	70.8	70.3	71.2	70.9	70.4	71.4	71.1	70.5	71.8
Median	**115.3**	**111.8**	**119.9**	**115.1**	**111.8**	**119.8**	**114.5**	**112.0**	**118.9**
97.5	173.2	162.9	180.2	171.5	159.3	178.3	165.3	159.2	169.6

[a] Total thyroxine = nmol/liter. To convert to mcg/dl, divide by 12.87.
[b] Disease-free population excludes those reporting thyroid disease, goiter, or taking thyroid medication.
[c] Reference population is the disease-free population without pregnancy, taking estrogen or androgen, no detectable thyroid antibodies, and without laboratory evidence of hypothyroidism or hyperthyroidism.

5.2, 2.4–11.5) ($P < 0.001$) but not TgAb ($P = 0.6$). The same relationship patterns existed in the disease-free population.

Relation of UI concentrations to TSH concentrations

When the geometric mean TSH concentrations were compared with iodine excretion, significantly higher TSH concentrations were found in persons with high I/Cr (>500 μg/g creatinine) than in persons with normal I/Cr excretion (50–500 μg/g creatinine) ($P < 0.02$), but not in people with low I/Cr. In the logistic regression model I/Cr >1000 μg/g creatinine was significantly associated with TSH concentrations >4.5 mIU/liter ($P < 0.001$). We found little or no difference in the mean TSH in people excreting normal UI (50–500 μg/liter) and those with either high or low UI. TSH was not a sensitive indicator of iodine deficiency in this population.

Discussion

This national survey demonstrates that average serum TSH concentrations and the prevalence of antithyroid antibodies are greater in women, increase with age, and are higher in whites and Mexican Americans than in blacks. Serum TSH values were also slightly higher in children aged 12–19 yr than in young adults aged 20–29 yr. These findings are in keeping with previous reports for older adults, women, and children (23–32).

A recent study of 25,862 people attending a state fair in Colorado found that 9.5% had TSH values >5.01 mIU/liter and 2.2% had TSH <0.3 mIU/liter. They found that only 60% of people taking thyroid medication had normal serum TSH values, which is similar to our findings among those who reported thyroid disease, goiter, or taking thyroid medications (33). We cannot explain the differences in the prevalence of thyroid disease between our findings and those seen in Colorado; however, they may relate to sampling methodology and regional differences. The NHANES sampling attempts to represent the U.S. population. For example, when we analyzed the rates of thyroid disease using only the white women studied without adjusting for the study sampling design, we get rates that approximate those found in Colorado.

Tunbridge *et al.* (34) in the Whickham, UK survey found that serum TSH levels did not vary with age in men but increased markedly in women aged greater than 45 yr. They found no increase in TSH with age in women in the absence of antithyroid antibodies. Our findings are somewhat different from those of Tunbridge *et al.* When we analyzed the population without antithyroid antibodies, the significant increase of TSH with age in both men and women persisted.

Serum TPOAb and TgAb concentrations increased with age. Antibodies were more prevalent in women than in men and less prevalent in black than in other ethnic groups. Increasing serum thyroid antibody prevalence with age has been found in other studies (31, 34–37). Although this cross-sectional study does not determine the risk for developing either subclinical hypothyroidism or progression of subclinical hypothyroidism to more clinically significant hypothyroidism, such a progression has been reported in some longitudinal studies (31, 38, 39).

The higher serum TSH concentration in whites than in blacks was previously reported in a small hospital-based population (40) and in an urban population among people over age 55 yr (41). In the present NHANES III study, TSH was higher in whites than in blacks even in the absence of thyroid antibodies and other risk factors. Although antibodies were less frequent in blacks, their association with TSH concentrations was much less in blacks than in whites. Environmental factors may be playing a role in these differences between whites and blacks, but analysis of region, poverty status, urban *vs.* rural residence failed to detect a significant

TABLE 6. Percentage of U.S. population with positive antithyroid antibodies[a] by thyroid status, age, gender, and ethnicity; NHANES III (1988–1994)

	Antithyroid peroxidase (TPOAb)												Antithyrogobulin (TgAb)											
	Total population						Disease-free population[b]						Total population						Disease-free population					
	Total		Male		Female		Total		Male		Female		Total		Male		Female		Total		Male		Female	
	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE
All ethnic groups																								
All ages	13.0	0.4	8.7	0.5	17.0	0.5	11.3	0.4	8.0	0.5	14.6	0.5	11.5	0.5	7.6	0.6	15.2	0.6	10.4	0.5	6.9	0.5	13.8	0.6
12–19	4.8	0.8	2.9	0.8	6.7	1.2	4.8	0.8	2.9	0.8	6.7	1.2	6.3	0.9	5.2	1.3	7.3	1.3	6.3	0.9	5.2	1.3	7.3	1.3
20–29	8.5	0.9	5.7	1.0	11.3	1.3	7.9	0.9	5.5	1.1	10.4	1.2	7.2	0.8	5.2	0.9	9.2	1.1	6.7	0.8	5.0	0.9	8.5	1.1
30–39	11.9	1.1	9.5	1.8	14.2	1.4	10.5	1.2	8.4	1.8	12.6	1.4	11.2	1.3	7.8	1.8	14.5	1.3	10.1	1.2	6.6	1.5	13.6	1.4
40–49	14.7	0.9	11.2	1.7	18.0	1.4	13.1	0.9	10.6	1.6	15.8	1.5	12.0	1.0	7.4	1.1	16.4	1.5	11.3	1.0	6.8	1.1	16.0	1.6
50–59	16.0	1.2	11.0	2.1	20.7	1.7	13.5	1.0	10.1	2.0	17.1	1.6	13.9	1.0	8.8	1.6	18.6	1.5	12.0	1.0	7.9	1.6	16.4	1.7
60–69	20.2	1.4	11.7	1.7	27.3	2.0	16.7	1.7	10.2	1.6	23.0	2.2	16.9	1.1	10.3	1.2	22.4	1.7	14.7	1.1	9.6	1.2	19.6	1.9
70–79	22.3	1.2	13.2	1.9	29.0	2.1	19.6	1.2	12.0	1.8	26.2	2.0	18.8	1.2	14.1	1.9	22.3	1.7	17.0	1.1	12.9	2.0	20.6	1.4
≥80	23.9	1.5	12.3	1.7	30.2	2.2	20.4	1.3	10.6	1.7	26.5	1.9	21.6	1.4	11.3	1.5	27.0	1.9	19.4	1.3	10.1	1.7	25.2	1.5
White, non-Hispanic																								
All ages	14.3	0.4	10.0	0.7	18.4	0.6	12.3	0.5	9.1	0.6	15.6	0.6	12.9	0.6	8.9	0.8	16.6	0.8	11.5	0.6	8.1	0.7	15.0	0.8
12–19	4.8	0.9	3.8	1.2	5.8	1.2	4.8	0.9	3.8	1.2	5.9	1.2	7.4	1.3	7.2	1.9	7.6	1.6	7.4	1.3	7.2	1.9	7.6	1.6
20–29	9.4	1.2	6.1	1.4	12.6	1.7	8.7	1.2	5.8	1.4	11.4	1.6	8.3	1.1	6.4	1.3	10.1	1.5	7.7	1.1	6.1	1.2	9.2	1.4
30–39	12.6	1.4	10.8	2.3	14.3	1.7	11.1	1.5	9.4	2.3	12.9	1.7	12.0	1.6	9.1	2.4	14.9	1.6	10.9	1.5	7.7	2.0	14.3	1.6
40–49	15.9	1.1	12.4	2.1	19.5	1.6	14.0	1.1	11.7	2.0	16.5	1.8	13.0	1.2	8.0	1.4	18.0	1.9	12.1	1.2	7.5	1.4	17.4	2.1
50–59	16.8	1.4	12.1	2.6	21.2	2.0	13.9	1.3	10.9	2.5	17.1	2.0	14.7	1.2	9.8	2.0	19.3	1.7	12.5	1.2	8.6	1.9	16.6	2.0
60–69	21.4	1.6	12.9	2.0	28.7	2.3	17.8	1.9	11.2	2.0	24.5	2.6	18.1	1.3	11.0	1.5	24.2	2.2	15.9	1.3	10.1	1.5	21.8	2.4
70–79	23.5	1.3	14.4	2.1	30.0	2.3	20.7	1.3	13.3	2.1	27.1	2.2	19.8	1.3	15.1	2.0	23.2	1.9	18.0	1.2	13.8	2.1	21.6	1.5
≥80	24.9	1.7	12.6	1.8	31.4	2.4	21.1	1.4	11.0	1.8	27.4	2.1	22.3	1.5	11.7	1.6	27.8	2.0	19.9	1.4	10.3	1.9	25.9	1.6
Black non-Hispanic																								
All ages	5.3	0.3	2.5	0.3	7.6	0.5	4.5	0.3	2.2	0.3	6.4	0.5	3.0	0.2	1.2	0.2	4.4	0.4	2.7	0.2	1.1	0.2	4.1	0.4
12–19	1.2	0.5	0.4	0.3	1.9	0.8	1.2	0.5	0.4	0.3	1.9	0.8	1.0	0.5	0.4	0.3	1.6	0.8	1.0	0.5	0.4	0.3	1.6	0.8
20–29	3.5	0.7	2.0	0.5	4.8	1.1	3.3	0.7	2.0	0.5	4.4	1.1	2.1	0.6	1.1	0.5	3.0	0.9	2.0	0.6	1.1	0.5	2.8	0.8
30–39	4.1	0.8	1.3	0.5	6.3	1.4	3.3	0.8	1.3	0.5	4.9	1.3	2.7	0.6	0.9	0.4	4.1	1.0	2.6	0.6	0.9	0.4	4.0	1.0
40–49	6.5	1.2	4.3	1.5	8.3	1.9	6.1	1.2	3.7	1.3	8.1	1.8	3.7	0.8	2.1	0.8	5.0	1.2	3.3	0.8	1.5	0.7	4.9	1.2
50–59	10.0	1.4	3.0	1.3	15.5	1.9	8.3	1.4	3.1	1.3	12.7	1.9	4.5	1.0	0.5	0.5	7.5	1.8	3.9	1.0	0.5	0.5	6.7	1.7
60–69	12.9	2.1	6.6	1.5	17.4	3.2	10.5	2.0	6.1	1.6	13.8	3.0	6.8	1.3	2.5	1.1	9.8	2.2	5.8	1.3	2.6	1.2	8.2	2.1
70–79	7.6	1.8	5.1	2.0	9.4	3.1	5.8	1.5	2.8	1.4	8.0	2.9	3.4	1.1	3.0	1.5	3.7	1.5	2.3	0.9	1.8	1.0	2.8	1.3
≥80	12.9	3.7	7.6	4.5	15.3	4.2	13.3	3.8	5.2	3.8	17.1	4.6	8.3	2.7	5.6	4.0	9.5	3.2	9.2	3.1	6.1	4.4	10.6	3.7
Mexican American																								
All ages	10.9	0.5	6.2	0.6	15.9	0.8	10.1	0.5	5.9	0.6	14.7	0.8	8.8	0.4	4.7	0.4	13.1	0.8	8.2	0.4	4.6	0.4	12.3	0.8
12–19	6.2	1.0	3.5	1.2	8.5	1.4	6.0	1.0	3.5	1.2	8.6	1.4	6.2	0.8	3.0	0.9	9.7	1.4	6.1	0.8	3.0	0.9	9.5	1.4
20–29	8.7	0.6	4.4	0.8	14.0	1.6	8.4	0.6	4.4	0.8	13.4	1.7	6.9	0.6	3.2	0.8	11.6	1.3	6.9	0.6	3.2	0.8	11.5	1.2
30–39	12.7	1.5	8.8	1.5	16.8	2.5	11.6	1.3	8.2	1.5	15.3	2.3	9.6	1.2	6.4	1.3	13.0	2.2	8.9	1.0	6.1	1.3	12.0	1.9
40–49	13.0	1.1	7.4	1.4	18.9	2.3	12.1	1.1	6.8	1.4	17.8	2.2	11.1	1.6	7.5	2.1	14.9	2.5	10.5	1.6	7.0	2.1	14.3	2.4
50–59	16.1	3.8	7.7	2.1	23.6	6.5	15.6	3.8	7.9	2.1	23.1	6.7	12.9	3.3	4.0	1.7	20.9	5.4	12.4	3.3	3.8	1.6	20.8	5.6
60–69	17.8	1.7	9.9	2.6	23.8	2.5	16.3	1.7	9.8	2.6	21.6	2.6	11.4	1.5	6.4	2.8	15.2	1.9	10.2	1.6	6.3	2.8	13.5	2.0
70–79	21.8	4.3	13.3	4.8	29.5	5.1	15.8	3.3	10.0	3.8	21.6	3.9	11.4	2.5	6.8	2.0	15.6	3.9	7.6	2.3	6.8	2.1	8.4	2.9
≥80	22.0	6.8	9.4	5.7	34.6	11.2	15.4	5.5	8.6	5.6	24.0	11.6	22.9	7.1	14.5	7.3	31.3	10.0	14.8	6.0	13.9	7.8	15.8	9.4

[a] TPOAb ≥0.5 U/ml. TgAb ≥1.0 U/ml.

[b] Disease-free population means those not reporting thyroid disease, goiter, or taking thyroid medications.

association other than race. This suggests that the thyroid-pituitary set-point for blacks may be different than for whites, due to as yet undefined factors. Although the group differences are significant, in view of the wide individual variation among persons in the various ethnic groups, it is probably inappropriate at this time to recommend separate clinical reference limits for blacks and whites. The relationship of laboratory to clinical status in blacks needs further study.

Our report has several limitations. First, total serum T_4 only was measured in this study so that thyroid status is less certain than if free T_4 concentration or index was available. Second, the study is cross-sectional and hence does not include individual changes over time. Third, 24-h urine samples could not be logistically carried out for a better assessment of iodine intake. Fourth, thyroid studies were not done on children under the age of 12 yr. Fifth, the study of noninstitutionalized people may have excluded some individuals at higher risk for thyroid disease. The oversampling of older people may have compensated for this to some extent. Finally, the presence of thyroid disease, goiter, or use of thyroid or other medication was self-reported and thyroid gland size (or the presence of goiter), and a detailed history was not obtained at the time of the examination.

The decrease in median UI in the U.S. between 1971–1974 and 1988–1994 prompted us to examine the relationship of low UI concentrations in individuals and evidence of hypothyroidism, but we found no association. The increase in the serum TSH concentration associated with a higher iodine intake may result from the adverse effect of excess iodine on thyroid function in persons with underlying thyroid disease such as Hashimoto's thyroiditis, history of subacute thyroiditis (5), or silent postpartum lymphocytic thyroiditis (42). The spot UI concentrations as collected are a better measure of the iodine nutrition in a population than in the individuals tested because they represent intake over a short period of time. TSH elevation is not a sensitive indicator of iodine deficiency in the U.S. at this time.

In conclusion, TSH and the prevalence of antithyroid antibodies are greater in females, increase with age, and are greater in whites and Mexican Americans than in blacks. TgAb alone in the absence of TPOAb is not significantly associated with thyroid disease. The lower prevalence of thyroid antibodies and lower TSH concentrations in blacks need more research to relate these findings to clinical status. The high prevalence of elevated serum TSH and antithyroid antibodies in the United States, especially in women and the elderly, suggests that thyroid disease should be considered during routine evaluation of this susceptible population and should be followed by appropriate detection and treatment. The finding that a large proportion of the U.S. population unknowingly have laboratory evidence of either hypothyroidism or hyperthyroidism supports the usefulness of screening for early detection (43). In the elderly and women of perimenopausal age, further research should be conducted to determine whether treatment of subclinical thyroid disease will be of benefit in preventing the associated diseases related to older age, such as osteoporosis, cardiovascular disease, hyperlipidemia, and neurologic disorders. Although we were not able to find a significant relationship between low iodine intake and elevated TSH in the present study, it is incumbent upon the U.S. to continue monitoring the status of iodine nutrition in the population.

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