intervention can lessen blood pressure during exercise seem indicated. This is especially true if data confirms mild to moderate exercise-induced elevation of blood pressure and greater than expected morbidity and mortality in patients with NIDDM who are to undergo moderately intense exercise programs.

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Received for publication 4 August 1989 and accepted in revised form 5 February 1990.

ACKNOWLEDGMENTS

This study was supported by the Department of Veterans Affairs and by a grant from the Upjohn Company. We acknowledge the cooperation of the patients and control subjects, and the valuable assistance of the nursing staff of the Special Diagnostic and Treatment Unit of the Veterans Administration Hospital, West Los Angeles Medical Center, Los Angeles, California.

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Screening for Thyroid Disease in Children With IDDM

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The aim of this study was to evaluate the usefulness of screening for thyroid disease by performing thyroid function tests and measuring thyroid autoantibodies in 371 children and adolescents with insulin-dependent diabetes mellitus (IDDM). We analyzed clinical data and results of serum thyroxine, triiodothyronine uptake, thyroid-stimulating hormone, and antibodies to thyroid microsomal antigen and thyroglobulin. Goiter was noted in 20% of subjects. Thyroid-specific autoantibody was positive in 19% of subjects. Twenty-seven subjects (7%) had thyroid dysfunction. Autoantibody testing identified subjects with thyroid dysfunction with a sensitivity of 50%, a specificity of 84%, a degree of misclassification of 17%, a positive predictive value of 13%, and a negative predictive value of 97%. We recommend that all children and adolescents be screened shortly after diagnosis of IDDM by determination of thyroid-stimulating hormone (measured by high-sensitivity assay) to identify thyroid dysfunction and by testing for antibody to thyroid microsomal antigen to characterize both risk of future thyroid dysfunction and the need for future testing.
***Diabetes Care* 13:801–803, 1990**

The association of insulin-dependent diabetes mellitus (IDDM) with thyroid disease, both hypothyroidism and hyperthyroidism, has been known for many years (1–3). Screening for thyroid disease was stressed recently in a position statement from the American Diabetes Association (4). However, a specific approach has not been recommended. The aims of this study were to determine the prevalence of both thyroid dysfunction and thyroid autoantibody positivity in children and adolescents with IDDM, relate biochemical findings to clinical features, evaluate the predictive value of autoantibody test results, and propose a protocol for screening for thyroid disease.

RESEARCH DESIGN AND METHODS

During a 12-mo period, 402 patients with IDDM had at least one admission to the pediatric service of the Diabetes Treatment Unit at New England Deaconess Hospital. All records were reviewed, and data were available on 371 subjects (212 girls, 159 boys). Their mean ± SD age was 13.9 ± 3.7 yr (range 3–22 yr). Duration of IDDM was 4.6 ± 4.2 yr (range 0–17 yr). The distribution of developmental stages (n = 330), based on the Tanner method of assessment, was I, 24%; II, 7%; III, 10%; IV, 22%; and V, 37%. Ten percent had a family history of IDDM among first-degree relatives, and 5% had a family history of autoimmune thyroid disease. Goiter was noted in 20%; most of these were small. Mean glycosylated hemoglobin level was 13 ± 3.0%, with a range of 6.3–22.6% (normal range 5.4–7.4%).

A fasting blood sample was drawn before breakfast on the morning after admission. Serum thyroxine was measured by radioimmunoassay (NML Tetra-Tab, Organon Teknika, Durham, NC), serum triiodothyronine uptake by determining unsaturated binding capacity of serum proteins (NML Tri-Tab, Organon Teknika), and serum thyroid-stimulating hormone (TSH) by radioimmunoassay (MAGIC TSH, Ciba Corning, Medfield, MA). Antibodies to thyroid microsomal antigen and thyroglobulin were determined by hemagglutination (Thymune-M and Thymune-T, Wellcome, Dartford, UK). Categorical variables were compared by the Mantel-

Haenszel χ^2-test. Bayesian analysis was used to determine the predictive value of autoantibody testing (5).

RESULTS

Thyroid organ-specific autoantibody was positive in 19.1%, thyroid microsomal antigen in 15.9%, thyroglobulin in 7.5%, and both in 4.3% (Table 1). There was no difference between sex. Fifty-one percent of patients with goiter had autoantibodies compared with 13% without goiter ($P < 0.0001$). Goiter was more common among subjects with a family history of autoimmune thyroid disease than in those without (42 vs. 18%, $P = 0.015$). The rate of autoantibody positivity increased significantly ($P = 0.014$) in midadolescence, with the prevalence according to Tanner staging I, 7.7%; II, 13.1%; III, 18.9%; IV, 25.7; and V, 19.7%. Thyroid dysfunction was noted in 27 subjects (7.3%). Two patients had newly diagnosed hyperthyroidism. Eleven patients were already receiving treatment for hypothyroidism; 82% were autoantibody positive. Fourteen patients had compensated hypothyroidism (elevated TSH with euthyroxinemia); treatment was deemed necessary in 2 patients.

Autoantibody testing had a sensitivity of 50% and a specificity of 84%. The positive predictive value (likelihood of thyroid dysfunction when the autoantibody test was positive) was 13%, and the negative predictive value (likelihood of thyroid dysfunction being absent when the autoantibody test was negative) was 97%. The degree of misclassification (false positives and false negatives as a percentage of the total number tested) was 17%, of which 13% were false negatives and 87% false positives. The predictive values improved when autoantibody positivity and goiter were combined.

DISCUSSION

In this study thyroid dysfunction was present in 7.3% of all patients screened, and 4.3% were diagnosed for the first time. Thyroid autoantibodies were detected in 19.1% of patients, more commonly directed against thyroid microsomal antigen than thyroglobulin. This rate of prevalence is similar to that reported by others and considerably greater than that of adolescents who do not have IDDM (3). In lymphocytic thyroiditis of childhood and adolescence, autoantibody titer levels tend to be lower than those in adults; intermittently, titers may even be negative. Repeated testing may be necessary to determine the exact prevalence of positivity. Thyroid autoantibody testing had a higher specificity (84%) than sensitivity (50%). A test with high specificity has greater clinical usefulness when the prevalence of disease is low (5).

Although not in use at the time of our study, many high-sensitivity assays for TSH are now routinely available. Unlike standard radioimmunoassays for TSH, the new immunometric assays can detect suppressed TSH levels. Studies in adults have shown their ability to detect states of hyperthyroidism and hypothyroidism on a single measurement (6). It is now recommended by many authorities that TSH, measured by a high-sensitivity assay, be the initial screening test whenever thyroid dysfunction is suspected.

It is suggested that initial screening be performed shortly after diagnosis, because thyroid dysfunction may precede the onset of IDDM (1,2). The presence of diabetic ketoacidosis, however, may confound interpretation of thyroid function tests (7). We recommend that the initial screening consist of both serum TSH level (measured by a high-sensitivity assay) and thyroid microsomal antigen antibody titer. Measurement of TSH is to identify thyroid dysfunction; testing for thyroid microsomal antigen antibody is to characterize the risk of developing thyroid dysfunction and thus the future need for thyroid function testing. Abnormal function tests, suggestive of either hypothyroidism (high TSH) or hyperthyroidism (low TSH), would require an immediate decision regarding further testing and management. Future testing in subjects with a high-risk profile, i.e., consisting of positive thyroid microsomal antigen autoantibody, goiter, or family history of autoimmune thyroid disease, should comprise repeated measurement of serum TSH levels at 2- to 3-yr intervals and sooner if necessary. Future testing in the remainder of subjects would be indicated only if there should be a clinical suspicion such as new onset of thyromegaly, a decrease in growth rate unexplained by poor glycemic control, or an inexplicable alteration of insulin requirement.

TABLE 1
Frequency of abnormalities in 371 patients

Autoantibody positivity	71 (19.1)
Thyroid microsomal antigen	59 (15.9)
Thyroglobulin	28 (7.5)
Both	16 (4.3)
Goiter	75 (20.2)
Thyroid dysfunction	27 (7.3)
Hyperthyroidism	2 (0.5)
Hypothyroidism (treated)	11 (3.0)
Hypothyroidism (compensated)	14 (3.8)

Percentages are in parentheses.

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Received for publication 24 October 1989 and accepted in revised form 3 January 1990.

ACKNOWLEDGMENTS

M.J.McK. was funded in part by the Robert and June Gurwin Research Fund at Henry Ford Hospital, Detroit, Michigan. R.H. is the recipient of a Capps Scholarship in Diabetes.

Parts of this study were published in abstract form in *Clin Res* 37:107A, 1988.

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