QUEENS PEDIATRIC SOCIETY

President: Dr. Samuel Dillon, 119-20 Rockaway Beach Blvd., Rockaway Park, N. Y.
Secretary: Dr. Moe Goldstein, 111-32 76th Ave., Forest Hills, N. Y.
Place: Seminole Club, 112th St. and 70th Rd., Forest Hills, N. Y. Time: Second Tuesday in October, December, February, and April.

RICHMOND PEDIATRIC SOCIETY

President: Dr. Hobart T. Dougan, 1832 Monument Ave., Richmond 20, Va.
Secretary: Dr. Robert A. Hoffman, 1001 W. Franklin St., Richmond 20, Va.
Place: Medical College Hospital. Time: 8 p.m., third Thursday of each month, except June, July, and August.

SAN ANTONIO PEDIATRIC SOCIETY

President: Dr. Edith M. Bonnet, 228 Medical Arts Bldg., San Antonio 5.
Secretary: Dr. Virginia S. Stovall, 1116 S. Texas Bldg., San Antonio 5.
Time: 7:30 p.m., supper, first Tuesday of each month.

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President: Dr. O. William Anderson.
President-Elect: Dr. Robert Tidwell.
Secretary-Treasurer: Dr. James L. Tucker.
Place: College Club. Time: 6:30 p.m., fourth Friday of each month from September to June.

ST. LOUIS PEDIATRIC SOCIETY

President: Dr. Maurice J. Lonsway.
Secretary: Dr. John C. Herwig.
Place: Candlelight House, 7800 Clayton Rd. Time: 6:30 p.m., second Thursday of each month from October to May, inclusive.

UNIVERSITY OF MICHIGAN PEDIATRIC AND INFECTIOUS DISEASE SOCIETY

President: Dr. Fred J. Chapin, 101 John St., Bay City.
Secretary-Treasurer: Dr. George H. Lowrey, University Hospital, Ann Arbor.
Place: University Hospital, Ann Arbor. Time: October, 1952.

WACO PEDIATRIC SOCIETY

President: Dr. J. M. Garrett, 1408 Austin Ave., Waco, Texas.
Secretary: Dr. C. G. Shellenberger, 1318 Austin Ave., Waco, Texas.
Place: 1917 Austin Ave., Waco, Texas. Time: Third Tuesday of each month.

WESTCHESTER COUNTY MEDICAL SOCIETY, PEDIATRIC SECTION

President: Dr. Herbert Kahan, 650 Main St., New Rochelle, N. Y.
Secretary: Dr. Elvira Ostlund, 64 Highland Rd., Rye, N. Y.
Place: The Roger Smith Hotel, White Plains, N. Y. Time: Four dinner meetings a year, November, February, April, and June.

WESTERN MICHIGAN PEDIATRIC SOCIETY

President: Dr. A. Morgan Hill, 310 Fulton, E., Grand Rapids.
Secretary: Dr. John C. Montgomery, 1810 Wealthy St., S.E., Grand Rapids.
Place: Two meetings in Grand Rapids, two elsewhere. Time: First Wednesday of October, November, April, and May.

WICHITA PEDIATRIC SOCIETY

President: Dr. Frank L. Menchan.
Secretary: Dr. R. C. Knappenberger.
Place: Homes of members. Time: 8:30 p.m., first Thursday, October through May.

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THYROTROPIC HORMONE IN INFANTS AND CHILDREN

Differentiation Between Primary and Hypopituitary Hypothyroidism

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AND
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SAN FRANCISCO

THIS PAPER presents data on the effect of the thyrotropic hormone[1] on I^{131} uptake by the thyroid for the differentiation of primary from secondary hypothyroidism in infancy and childhood.

While hypothyroidism in infancy and childhood has been the subject of much clinical research since the turn of the century, only minor amendments have been made to the excellent clinical classification presented by Pineles in 1902.[2] Much has been learned, however, about the chemistry and physiology of pituitary and thyroid function, and from these certain practical laboratory aids in diagnosis have been standardized and are available to most clinicians for routine use. Among these, in hypothyroidism, are roentgenographic evidence of retardation of skeletal maturation, failure of linear bone growth, epiphyseal dysgenesis,[3] chemical and metabolic evidence of lowered basal metabolic rate,[4] low serum alkaline phosphatase,[5] elevated serum cholesterol,[4] and hypercarotinemia.[6]

During the past decade the practical and accurate determination of the serum protein-bound iodine concentration has added a comparatively direct method of

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1. Thyrotropic hormone, a lyophilized, pyrogen-free product, was furnished through the courtesy of the Armour Laboratories, Chicago. In no case was either a local or a generalized reaction encountered following its dilution with sterile isotonic sodium chloride solution and intramuscular injection.

2. Pineles, F.: Über Thyroplasie (kongenitales Myxödem) und infantiles Myxödem, Wien. klin. Wchnschr. 16:1129, 1902.

3. Reilly, W. A., and Smyth, F. S.: Stippled Epiphyses with Congenital Hypothyroidism (Cretinoid Epiphyseal Dysgenesis), Am. J. Roentgenol. 40:675, 1938. Wilkins, L.: Epiphysial Dysgenesis Associated with Hypothyroidism, Am. J. Dis. Child. 61:13, 1941.

4. Wilkins, L.; Fleischmann, W., and Block, W.: Hypothyroidism in Childhood: The Basal Metabolic Rate, Serum Cholesterol and Urinary Creatine Before Treatment, J. Clin. Endocrinol. 1:3, 1941.

5. Talbot, N. B.; Hoeffel, G.; Schwachman, H., and Tuohy, E. L.: Serum Phosphatase as an Aid in the Diagnosis of Cretinism and Juvenile Hypothyroidism, Am. J. Dis. Child. 62:273, 1941.

6. Escamilla, R. F.: Carotinemia in Myxedema: Explanation of Typical Slightly Icteric Tint, J. Clin. Endocrinol. 2:33, 1942.

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measurement of one aspect of thyroid function.[7] With the development of isotopic techniques, I^{131} uptake and excretion studies have similarly added much to our present concepts of thyroid function and have been used in many centers as an aid in diagnosis and treatment of thyroid disorders.[8]

While the above diagnostic methods have aided in the clinician's identification of hypothyroidism per se, they generally have failed to differentiate between hypothyroidism due to thyroid failure, or athyrosis (primary hypothyroidism), and hypothyroidism due to deficiency of anterior pituitary thyrotropic hormone production (secondary hypothyroidism). In general, it has been customary to attempt to make this differential diagnosis through a search for signs of other pituitary deficiencies by a study of other trophic hormones, such as the gonadotropins and corticotropin (ACTH), and of growth. If other pituitary deficiencies are present, it is taken as evidence of pituitary failure. Errors may arise from such parallelism, however, since such deficiencies may be caused by myxedema.[9] This was found to be true in one of the cases to be reported (A. P.). In a hypothyroid patient growth failure out of proportion to clinical and chemical indications of hypothyroidism and poor growth following thyroid therapy suggest the presence of hypopituitarism.

An attempt to differentiate between primary and secondary hypothyroidism reported here is based upon the pronounced effect of parenterally injected thyrotropic hormone on I^{131} uptake in thyroids of patients with pituitary deficiency, in contrast to the slighter effect on those with adequate pituitary function.

EXPERIMENTAL PROCEDURES

Description of Patients.—Six clinically hypothyroid children without goiter were selected for study from the patients attending the University of California Pediatric Clinic in San Francisco. Five clinically euthyroid children were chosen for control. Among the controls one patient had diabetes (P. B.), one was a dwarf (L. T.), two were mentally defective (S. H. and R. E.), and one had Legg-Calvé-Perthes disease (P. F.). The dwarf was normal in all respects, except for stature. The results of studies of his intelligence quotient, body proportions, dental and bone age, gastrointestinal tract, and genitourinary and cardiovascular systems were all within normal limits. Among the hypothyroid patients two were presumed to be athyrotic cretins (R. S. and R. M.); one (A. P., 9 years of age) became myxedematous spontaneously at 5 years of age and remained untreated for four years before investigation. Of the patients with pituitary hypothyroidism studied, one was a dwarfed infant (T. W.) and the other a 15-year-old girl with an eight-month history suggesting anorexia nervosa (B. P.).

7. Riggs, D. S.; Gildea, E. F.; Man, E. B., and Peters, J.: Blood Iodine in Patients with Thyroid Disease, J. Clin. Invest. **20**:345, 1941. Rapport, R. L., and Curtis, G. M.: The Clinical Significance of the Blood, J. Clin. Endocrinol. **10**:735, 1950. Mann, E.; Pickering, D. E.; Walker, J., and Cooke, R. E.: Butanol-Extractable Iodine in the Serum of Infants, Pediatrics **9**:32, 1952.

8. (a) Miller, E. R.; Dailey, M. E.; Holmes, A. V.; Alexander, G. L., and Sheline, G.: Studies with Radioiodine: I. Function and Rate of I^{131} Uptake of Thyroid, Radiology **57**:37, 1951. (b) Miller, E. R.; Dailey, M. E.; Soley, M. H.; Foreman, N.; Holmes, A. V.; Alexander, G. L., and Sheline, G. E.: Studies with Radioiodine: II. Treatment of Patients with Hyperthyroidism by I^{131}, ibid. **57**:227, 1951. (c) Miller, E. R., and Sheline, G. E.: Studies with Radioiodine: III. Problem of Dosage in the Treatment of Hyperthyroidism, ibid. **7**:722, 1951. (d) Hamilton, J. G.; Soley, M. H.; Reilly, W. A., and Eichorn, K. B.: Radioactive Iodine Studies in Childhood Hypothyroidism, Am. J. Dis. Child. **66**:495, 1943.

9. Stafland, H., and Lerman, J.: Function of Adrenal Cortex in Myxedema, with Some Observations on Pituitary Function, J. Clin. Endocrinol. **10**:1401, 1950.

Studies of Patients.—All the patients were studied clinically, and determinations of bone age and protein-bound iodine were made for each. Pituitary-adrenal function studies were made for three of the controls and all of the hypothyroid patients (Table 1).[10] At least two of the pituitary-adrenal function tests were carried out on patients designated "normal" in Table 1. Three of the hypothyroid patients had normal results of pituitary-adrenal function studies, and three had results in the abnormal range as follows:

PATIENT A. P.—(1) The 24-hour urinary 17-ketosteroid excretion was low: 1.1 mg. (normal range 2 to 5 mg. per 24 hr.); (2) circulating eosinophiles did not drop significantly (156 to 147 per cubic mm.) four hours after administration of epinephrine or four hours after administration of corticotropin (234 to 184 per cubic mm.); (3) there was no significant increase in urinary 17-ketosteroid excretion after 48 hours of administration of corticotropin.

It is interesting to note that the above pituitary-adrenal test pattern reverted to normal on retesting, after the patient received a three-month period of thyroid medication followed by 30 days without thyroid. This suggests that her originally subnormal adrenal cortical function was secondary to myxedema and that the adrenals regained competency following relief of her myxedema.

TABLE 1.—*Collateral Data on Patients Receiving Thyrotropic Hormone*

Diagnosis	Patient	Age: Chronological, Yr.	Age: Onset of Symptoms	Bone Age	Basal Metabolic Rate	Pituitary-Adrenal Function	Urinary Gonadotropin, Mouse Units	Protein-Bound Iodine (Serum) γ/100 Cc.
Euthyroid		1	Dwarf from 8 mo.	Normal	[illegible]	.....	...	6.7
		4	.....	Normal	..	Normal	...	5.5
		1½	.....	Normal	..	.....	...	4.7
		10	.....	Normal	..	Normal	...	5.0
		1½	.....	Normal	..	Normal	...	5.0
Hypothyroid		1⅝	4 mo.	8 mo.	..	Normal	...	5.5
		1½	1½ mo.	8 mo.	..	Normal	...	5.0
		5/12	1½ mo.	0	..	Normal	...	5.0
		9	6 yr.	6 yr.	−25%	Abnormal	<5	5.1
		1	8 mo.	8 mo.	..	Abnormal	<5	5.5
		15	14 yr.	Normal	−48%	Abnormal	<5	5.5

PATIENT T. W.—This dwarfed and fragile one-year-old infant demonstrated less than 50% decrease in circulating eosinophiles four hours after administration of epinephrine, while she demonstrated a significant (50% decrease) response to corticotropin. After thyroid therapy she demonstrated much less growth and osseous maturation than would be customarily found in a cretin infant. These findings support the impression of hypopituitarism.

PATIENT B. P.—This 15-year-old girl was well until eight months before investigation, at which time amenorrhea and anorexia associated with marked weight loss developed and her condition was diagnosed as anorexia nervosa. Neurological investigation at the time of our study revealed no evidence suggesting disease of the central nervous system. She demonstrated an adequate response to both epinephrine and corticotrophin by more than a 50% reduction in circulating eosinophiles. Twenty-four hour urinary 17-ketosteroid excretion was 2.4 mg., which

10. When there was any question relating to the integrity of pituitary-adrenal function, the following determinations were made: (1) the determination of 24-hour urinary excretion of 17-ketosteroids and Compound F (17-hydroxycorticosterone); (2) the response of circulating eosinophiles to epinephrine in the following doses: 0.03 cc. 1:1,000 epinephrine per kilogram until 0.5 cc.; 0.5 cc. for patients weighing 15 to 30 kg.; 0.75 cc. for larger patients; (3) the response of circulating eosinophiles to parenterally injected corticotropin (ACTH), and (4) the 48-hour response to corticotropin injection as measured by 17-ketosteroid and Compound F excretion in the urine.

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is lower than normal for a girl in this age group. Forty-eight hours after corticotropin therapy her urinary 17-ketosteroid excretion rose precipitously and subsequently returned to her originally low value within 24 hours. Compound F (17-hydroxycorticosterone) excretion followed a similar pattern.

I^{131} AND THYROTROPIC HORMONE STUDIES

Following an 8- to 12-hour fast, each child received from 15 to 40 μc of carrier-free[11] I^{131} orally or through a polyethylene tube. The per cent of uptake of the I^{131} in the thyroid was determined at 0, 2, 6, and 24 hours following administration. The techniques used in handling and counting I^{131} were those described in a previous report from this laboratory, with but slight modification.[8a] The initial 24-hour I^{131} uptake by the control group was from 12 to 20%. The initial 24-hour I^{131} uptake by the thyroid both in cases of hypopituitary hypothyroidism (T. W. and B. P.) and in one case of primary hypothyroidism (L. B.) fell within the range of the euthyroid group (12 to 20%). The uptake of I^{131} in the remaining three hypothyroid patients was very small. I^{131} uptake by the thyroid in hypothyroidism, primary or secondary, may therefore be indistinguishable from that in euthyroid children. Significant I^{131} uptake in cretins has previously been reported by this and other clinics.[12]

TABLE 2.—*Thyrotropic Hormone Dosage (Given Intramuscularly Every 12 Hours × 4)*

Patient's Weight, Kg.	Thyrotropic Hormone, Mg.
5	5
5-15	7.5
15-30	10
30+	15

Twenty-four hours following completion of the initial I^{131} uptake studies, thyrotropic hormone therapy was begun and was continued over a period of 48 hours for all patients whose cases are reported. This was followed by a repetition of the I^{131} uptake study, employing the same dosage and technique used in the initial study. The quantity of thyrotropic hormone injected per dose is shown in Table 2.

RESULTS AND COMMENT

Data showing the 24-hour thyroid uptake of I^{131} before and after 48 hours of thyrotropic hormone administration are presented in the graph.

Pretreatment per cent uptake (24 hours) of I^{131} by the thyroid is represented in vertical clear columns, below zero in each case. Per cent uptake (24 hours) of I^{131} by the thyroid after 48 hours of thyrotropic hormone therapy is graphed as the entire vertical column, and the difference between the two, per cent increase following administration of thyrotropic hormone, is graphed above zero in the stippled portions of the columns. Individual cases are graphed according to clinical impression in the bottom horizontal column.

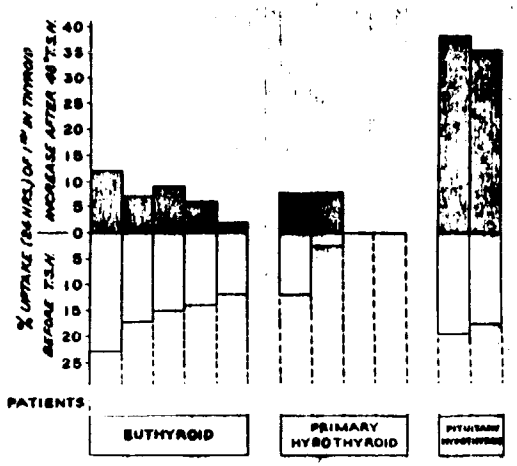
In these euthyroid patients the 24-hour thyroid uptake of I^{131} increased from 2 to 12% after administration of thyrotropic hormone.

11. Radioactive I^{131}, free from nonradioactive iodine, permits labeling of the extra thyroidal morganic iodine pool without contributing to it.

12. Lerman, J.; Jones, H. W., and Calkins, E.: Studies on 2 Sporadic Cretinous Brothers with Goiter, Together with Some Remarks on the Relation of Hyperplasia to Neoplasia, Ann. Int. Med. 25:677, 1946. Stanbury, J. B., and Hedge, A. N.: A Study of a Family of Goitrous Cretins, J. Clin. Endocrinol. 10:1471, 1950. Footnote 8d.

The data from studies of the hypothyroid patients divide themselves into two groups. In the first, primary hypothyroidism, the response to the administration of thyrotropic hormone is in the normal range (2 to 12%); in the second group, secondary hypothyroidism, the response is over three times as high (35 to 38%).

One patient with primary hypothyroidism (L. B.) was not recognized to be hypothyroid until she demonstrated a dramatic response to thyroid therapy. Her protein-bound iodine determination was 3.8 γ per 100 cc. An increase of 8% was observed in her 24-hour I^{131} uptake after administration of thyrotropic hormone. Another patient with primary hypothyroidism (R. M.) was an 18-month-old cretin whose clinical diagnosis was made at the age of 2 months. He had been inadequately treated from the time of diagnosis until three weeks before this study was begun, at which time therapy was discontinued. There was no significant uptake



Thyrotropic hormone effect on uptake (24 hour) of I^{131} in thyroid.

of I^{131} by the thyroids in the remaining children with primary hypothyroidism (A. P. and R. S.).

The two hypopituitary children with secondary hypothyroidism (T. W. and B. P.) demonstrated an increase of over 35% in their uptake of I^{131} after administration of thyrotropic hormone. Similar results have been reported in the cases of three adults by Querido and Stanbury.[13] Thus, the use of I^{131} uptake as influenced by the administration of thyrotropic hormone is a practical diagnostic procedure which served to differentiate primary from secondary hypothyroidism in these patients. In accord with previous observations, we have found that the thyroid uptake of I^{131} in primary hypothyroidism may fall within the range for euthyroid patients.

13. Querido, A., and Stanbury, N.: The Response of the Thyroid Gland to Thyrotropic Hormone as an Aid in the Differential Diagnosis of Primary and Secondary Hypothyroidism, J. Clin. Endocrinol. 10:1192, 1950.

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It would seem to us that carrier-free I^{131} uptake represents thyroid uptake of the extrathyroidal inorganic iodine pool. Such uptake need not be directly related to production and/or release of thyroid hormone. It is obviously influenced by the dimensions and concentration of the immediately available 24-hour iodine pool. Thyroid size and exposure to the pool are also determinants. It is also influenced directly by the thyrotropic hormone.

While the per cent of the iodine pool taken up by the thyroid in the hypopituitary-hypothyroid group during the pretreatment period was found comparable to the per cent uptake in the euthyroid group, following thyrotropic hormone administration similar comparison revealed greatly increased uptakes in the hypopituitary hypothyroid group. Such observations suggest existence of a small iodine pool in the hypopituitary hypothyroid.

SUMMARY AND CONCLUSIONS

The effect of thyrotropic hormone as measured by an increase in I^{131} uptake has been measured in five euthyroid and six hypothyroid children.

Parenteral administration of thyrotropic hormone for 48 hours to five euthyroid children was followed by an increase in thyroid I^{131} uptake by 3 to 12% over their preceding 24-hour thyroid uptake of I^{131}.

Two of four hypothyroid children, assumed to have primary end-organ deficiency, demonstrated no I^{131} uptake either before or after thyrotropic hormone administration, while the remaining two demonstrated an increase of 8% of I^{131} uptake following thyrotropic hormone administration.

In contrast, similar administration of thyrotropic hormone in two hypothyroid children who demonstrated collateral signs of pituitary insufficiency was followed by an increase of from 35 to 38% over their previously determined thyroid I^{131} uptake. This suggests a method for differentiating primary from secondary hypothyroidism in childhood.

TRIGGER THUMB IN INFANTS

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AND
WILLIAM E. JENSEN, M.D.
HONOLULU, T. H.

A TRIGGER mechanism is one in which motion is carried to a certain point, at which a resistance is met, but further motion carries it beyond the resistance with a snapping sensation or a definite "give." In the trigger thumb the motion from flexion to extension is most frequently blocked at about 150 degrees, and then further pressure overcomes the resistance and full extension is obtained. This works in a similar way with motion from full extension to flexion, meeting the same resistance. When the child is seen by the physician, the thumb is frequently locked with the distal phalanx in flexion. However, the history given by the parents shows that the typical trigger mechanism was present at the onset, but gradually the resistance increased until the phalanx locked in flexion. In our series of cases seven of the nine trigger thumbs were in the persistent locked state when the condition was observed. Finding the thumb in this state would give reason for an error in diagnosis. During the time these cases of trigger thumbs were collected and observed the same mechanism was not seen in any other digits in children coming to the Shriners' Hospital for Crippled Children.

This condition has also been called snapping thumb and stenosing tenovaginitis. It does not appear progressive after the persistent locking occurs, and except in the report by Rose,[1] writers do not describe any inflammatory changes, but only hyperplastic changes. An example of the stable nature of the condition is the case reported by Compere[2] of a 24 year-old woman who had had the condition since she first noticed it at 4 years of age. In this particular case there had been no evidence of progressive changes. This is especially true because of the fact that there were no progressive degenerative changes that could not be relieved by simple incision of the tendon sheath, which is exactly the same as in infants.

Numerous different diagnoses are made when the true nature of the condition is not recognized. The commonest ones are congenital contracture of the thumb, chronic dislocation of the interphalangeal joint, and ankylosis of the interphalangeal joint. The lack of reports of many series of cases would suggest that this is not a frequently diagnosed condition, or, as considered by some writers, is somewhat rare. The adult type of trigger finger is fairly frequent, but the involvement of the thumb in adults is considered rare. The case reported by Compere[2] is the only one

From the Shriners' Hospital for Crippled Children.

1. Rose, T. F.: Bilateral Trigger Thumb in Infants, M. J. Australia 1:18 (Jan. 5) 1946.
2. Compere, F. L.: Bilateral Snapping Thumbs, Ann. Surg. 97:773 (May) 1933.