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Thyroid Size may be considered an Additional Useful Peripheral Parameter for Rapid Assessment of the Activity of Acromegaly

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Abstract: **Objective**: Acromegaly is frequently associated with the existence of thyroid gland diseases. Long-term stimulation of the follicular epithelium by growth hormone (GH) and insulin-like growth factor 1 (IGF-1) can result in thyroid function problems, an increase in thyroid mass, and the development of goiter. A prospective study evaluating the thyroid size and morphology and correlating with the activity of acromegaly (include GH, IGF-1). The study was conducted in the National Diabetes Center / AL-Mustansiryah University from January 2022 – April 2023. **Subjects and methods**: Ultrasound measurements were done for thirty acromegalic patients 18 male , 12 female , age range 24- 72 years (mean age S.D 45.63 ± 11.96) whom had active disease(mainly newly diagnosed) for different duration of disease (1-30 years, S.D 45.63 ± 11.96) and under treatment with somatostatin analogues (Sandostatine LAR , 20 mg every 28 days), these are examined consecutively every three time (every three month)for six months (baseline =initial diagnosis, after 3 month with treatment and after 6 month with treatment) by ultrasound for the assessment and verify for thyroid volume and morphology, and correlate these variables with the marker of response to treatment by LAR and at each session of exam, GH test and IGF-1 serum level was measured at each visit and correlate with thyroid size. **Results:** Thyroid size was significantly related with GH, and disease duration after 6 months' follow-up, the thyroid size decreased significantly ($p<0.05$). However, no significant changes were found in Thyroid size after 3 months. Significant difference was observed in Growth Factor Level (IGF-1) and Growth Hormone Level (GH) after 6 months follow up. **Conclusions:** We developed a study based on the findings of this investigation regarding the development of goiter in acromegaly. Initially, high IGF-I levels cause diffuse thyroid hypertrophy.

Keywords: Insulin-like growth factor 1, Acromegaly, Thyroid disease, Goiter.

INTRODUCTION

Acromegaly is a chronic condition characterized by a pituitary adenoma that causes continuous hypersecretion of growth hormone (GH) and a subsequent increase in insulin-like growth factor-1 (IGF-1). The increasing occurrence of thyroid lesions in acromegaly patients raised researchers' interest [Melmed, S. *et al*., 1990]. The relationship between acromegaly and goiter has long been established. Rolleston noted in 1936 that in acromegaly, "the thyroid is palpably enlarged in a significant proportion, perhaps a quarter, of the cases." Other investigations, based on clinical examination, have indicated a prevalence of goiter in acromegaly ranging from 25 to 71%. It appears that thyroid enlargement in acromegaly is caused by chronically high IGF-I levels [Wuster, C. *et al*., 1991]. As a result, people with acromegaly may experience increased thyroid growth. Thyroid function in acromegaly has also been extensively studied. Despite the fact that GH has been shown to alter the activity of thyroxine deiodinase, which may affect thyroid hormone levels in acromegaly patients, most acromegaly patients are euthyroid [Cannavò, S, 2000]. The hypothalamic–pituitary–thyroid axis (HPT axis for short, also known as thyroid homeostasis or thyrotropic feedback control) is part of the endocrine system responsible for the regulation of metabolism. The hypothalamus senses low circulating levels of thyroid hormone (T3 and T4) and responds by releasing thyrotropin-releasing hormone (TRH). The TRH stimulates the pituitary to produce thyroid-stimulating hormone (TSH). The TSH, in turn, stimulates the thyroid to produce thyroid hormone until levels in the blood return to normal. Thyroid hormone exerts negative feedback control over the hypothalamus as well as anterior pituitary, thus controlling the release of both TRH from hypothalamus and TSH from anterior pituitary gland [Melmed, S. *et al*., 1990]. The Pituitary gland integrates hormonal signals that control adrenal, thyroid, reproductive, growth, and metabolic functions. Distinct cellular compartments within the pituitary gland secrete highly specific trophic hormones in response to hypothalamic, intrapituitary, and peripheral hormonal and growth factor signals [Wuster, C. *et al*., 1991]. Acromegaly is a syndrome that results when the anterior pituitary gland produces excess growth hormone (GH) after epiphyseal plate closure at puberty. A number of disorders may increase the pituitary's GH output, although most commonly it involves a GH-producing tumor called pituitary adenoma, derived from a distinct type of cell (somatotrophs). Acromegaly most commonly affects adults in middle age and can result in severe disfigurement, complicating conditions, and premature death if untreated. Because of its pathogenesis and slow progression, the disease is hard to diagnose in the early stages

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and is frequently missed for years until changes in external features, especially of the face, become noticeable [Al Dallal, S, 2018; Banerjee, A. *et al*., 2003]. The incidence of acromegaly is 5 cases per million per year and the prevalence is 60 cases per million. Clinical manifestations in each patient depend on the levels of GH and IGF-I, age, tumor size, and the delay in diagnosis. Manifestations of acromegaly are variable and include acral and soft tissue overgrowth, joint pain, diabetes mellitus, hypertension, and heart and respiratory failure [Gloria, L. *et al*., 2012]. Acromegaly is a disabling. The diagnosis is based primarily on clinical features and confirmed by measuring GH levels after oral glucose loading and the estimation of IGF-I. It has been suggested that the mortality rate in patients with acromegaly is correlates with the degree of control of GH, tight control of GH improve survival [Holdaway, I. M. *et al*., 2004; Isidro, M. L. *et al*., 2005]. Normal thyroid gland is located in the anterior inferior neck. It is divided into lobes resting on either side of the trachea. The lobes are connected at their lower third by thin isthmus that crosses anterior to the trachea. Immediately anterior to the thyroid are the thin strap muscles (sternohyoid, sternothyroid, and omohyoid). Lateral to the thyroid are the bulkier sternocleidomastoid muscles. The longus colli muscles rest immediately anterior to the vertebrae and posterior to each lobe of the thyroid. The common carotid arteries are located lateral to each thyroid lobe, and the jugular veins are anterior and lateral to the carotids. In the adult the thyroid measures 4-6 cm in length and 1.3-1.8 cm in antero-posterior and transverse diameter [Laszlo, H. *et al*., 1983]. The isthmus measures up to 3 mm in thickness, thyromegaly is present whenever the transverse or anteroposterior diameter exceedes 2 cm or when parenchyma extends anterior to the carotid [Al Dallal, S, 2018]. So the normal thyroid volume ranging (6.46 - 9.70 ml). The aim of the present study was to evaluating the thyroid size and morphology and correlating these ultrasonic finding with acromegalic control based on GH, and IGF-1 levels

SUBJECTS AND METHODS

The study included 30 patients with acromegaly (12 females and 18 males), their age range between 24- 72 years old with mean age of (45.63 ±11.96 years). The study was carried out in accordance with medical ethics guidelines, and all subjects gave their consent. The study was conducted in the National Diabetic Center/ Mustansyriah University between January 2022 – April 2023. Exclusion criteria were: those who having undergone thyroidectomy, radiotherapy, suspicious thyroid nodule, and initially six patients were exempted from this study were planning for them to get Sandosatatine LAR 40mg and show marked discordance of GH and IGF-1 level, in spite of evident decrease thyroid size. Thyroid volume was determined and realize using ultrasonography Mindray DC-60, with a linear probe 7L4A (F 6.6-13.5 MHz). Transverse thyroid slices were imaged at 10-mm intervals. The area of each segment was determined by computer after digitizing the shape of the gland using a cursor, and the sum of the areas formed the estimated thyroid volume, which was expressed in milliliters. During this study realize to manual measurement by taking the maximum dimensions of thyroid panels: length (L), width (W) and thickness (T). Additionally, it evaluated echogenicity as well as to states a presence of goiters changes in the glandular tissue.

Thyroid volume was calculated using Braun expression [William, D. M. *et al*., 2003]:

$V\ US = 0.479 \cdot L \cdot W \cdot T$ ……………………..… (1)

Each lobe was calculated its volume and then thyroid lobes volume added together [Lucas, K. J, 2000]:

$V\ Thyroid = V\ RL + V\ LL$ …………………..…. (2)

The method for the quantitative determination of IGF-1 and GH level is one –step sandwich Chemilumimnescence immunoassay (CLIA) by LIAISON Analyzer in our center. Growth hormone and IGF-1 are studied for each patient and the goal of GH is < 0.4 ng / ml, while IGF-1 should be age and sex matched as for non-acromegalic counterparts.

Statistical Analysis

The data were analyzed in Microsoft Office Excel 2010 and presented as mean, and standard deviation. The unpaired t-test was used to determine significance, and a p value of 0.05 was considered significant.

RESULTS

Thirty patients with acromegaly 18 males, 12 females, mean age (45.63 ±11.96years) who meet the inclusion criteria were enrolled in the study. The mean period of follow-up was 7.76±7.71 months. Table 1.

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Table 1: Baseline characteristics of study sample (n=30).

Variables		Values
Age (years)/ mean (±SD)		45.63 ±11.96
Gender	Males/ n (%)	18 (60%)
	Females/ n (%)	12(40%)
Disease duration (months/mean (±SD)		7.76 ±7.71

After follow-up, 30 patients were compared their result before and after treatment (baseline, after 3-month treatment and after 6-month treatment). For all participants, the growth factor level (IGF-1) (ng/ml) decreased significantly in all patients (535.46 ± 276.90, 443.23 ± 247.23) after 3months and 6 months respectively, p< 0.05), table 2. However, no significant changes were found in Growth Hormone Level (GH) (ng/ml) after 3 months session, were at 6 months session of follow-up , GH decreased significantly, GH decreased significantly from baseline 7.27 ±11.43 to 2.53 ± 4.64 with ($p < 0.05$). The change of Thyroid Size (TS) showed a declined trend after 3months but were not significant, the mean was 18.98 ±9.36, while after 6 months the TS decreased significantly from 22.53 to 16.98 ± 8.22, ($p < 0.05$). Table 2.

Table 2: Growth hormone, IGF-1, and thyroid volume at baseline, after 3month and 6 months of Octreotide use

Variables	Before treatment	After 3 months	After 6 months
IGF (ng/ml)	733.5 ± 431.34	535.46 ± 276.90	443.23 ± 247.23
GH (ng/ml)	7.27 ±11.43	4.29 ±8.17	2.53 ± 4.64
TS (ml)	22.53 ±10.76	18.98 ±9.36	16.98 ± 8.22

Both figures 1 and 2 show the relationship between IGF, and GH with thyroid size before and after treatment for consecutive three and six months, with a clear descent in the curve after treatment compared to the baseline before treatment.

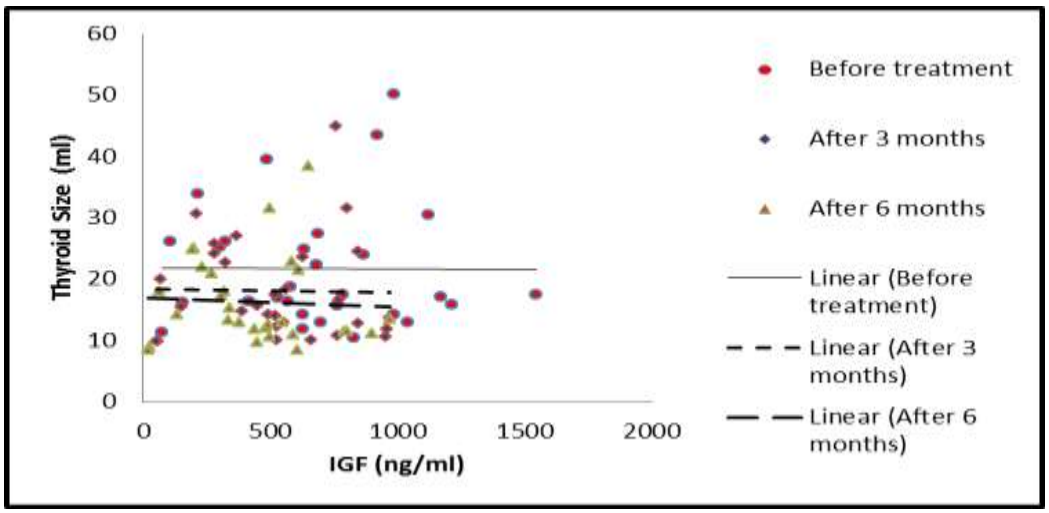

Figure 1: Relationship between IGF (ng/ml) and Thyroid Size (ml) before and after treatment (3 and 6 months)

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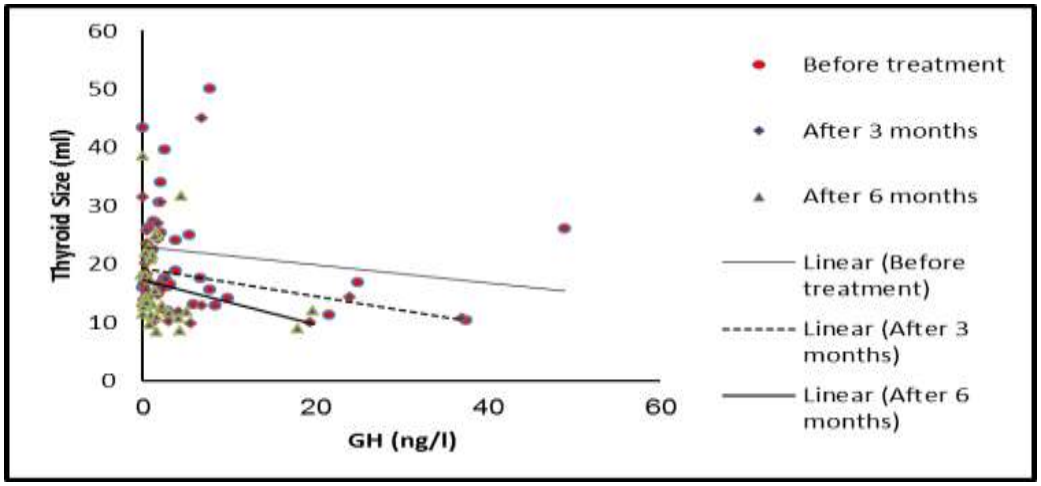

Figure 2: Relationship between GH (ng/ml) and Thyroid Size (ml) before and after treatment (3 and 6 months).

In Figure 3, the thyroid volume was correlated with the estimated duration of acromegaly (r^2=0.1461, p<0.0001)

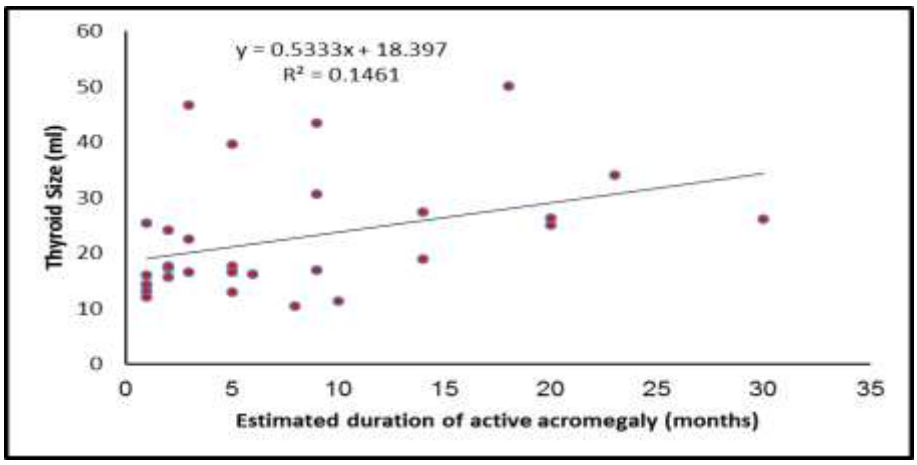

Figure 3: Correlation between thyroid size (ml) and estimated duration of disease (months).

Table 3 shows the mean thyroid size was found to have no significant difference between males and females (19.97 ± 11.05 ml vs. 16.72 ± 6.40ml), after 3 months, and there was also no significant difference after 6 months (17.70 ± 9.74ml vs 15.09 ± 5.78 ml) respectively, p > 0.05. The mean change in GH (ng/ml) for males and females was (4.23 ± 6.73 vs 4.51 ±10.26) respectively, with insignificant p value > 0.05, after 3 months. Also, there was an insignificant change in GH (ng/ml) after 6 months for both males and females, with a mean of (3.48 ± 5.85 vs 1.22 ± 0.64) respectively. The observed change between male and female in IGF (ng/ml) after 3 and 6 months shows a highly decreased in males compared with females, which is highly significant, table 3.

Table 3: IGF-1, GH and thyroid volume after enrollment, 3 months and 6 months after Octeriotide LAR injection in men and women

Variables	Before treatment	After 3 months	After 6 months
Male (mean ±SD)			
IGF (ng/ml)	801.61 ± 502.44	538.05 ± 289.16	439.44 ± 235.08
GH (ng/ml)	8.74 ± 12.18	4.23 ± 6.73	3.48 ± 5.85
TS (ml)	23.63 ± 12.19	19.97 ± 11.05	17.70 ± 9.74
Female (mean ±SD)			
IGF (ng/ml)	691.5 ± 236.90	589.33 ±233.99	494.25 ± 248.74
GH (ng/ml)	5.17 ±10.28	4.51 ±10.26	1.22 ± 0.64
TS (ml)	19.58 ± 8.75	16.72 ± 6.40	15.09 ± 5.78

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DISCUSSION

This study investigated and clarified changes in thyroid structure, mass and function and correlate with GH and IGF-1 levels in acromegalic patients at National Diabetic Center/ Mustansyriah University. Our investigation found that lowering GH levels following acromegaly treatment could influence the size of an enlarged thyroid and alter thyroid function. Thyroid disease, particularly goiter, is a common acromegaly consequence. Previous studies revealed that goiter occurs in 20%–90% of acromegaly patients, typically manifesting as thyroid enlargement. The apparent increased prevalence recently observed can be attributed to the use of highly sensitive thyroid ultrasonography [Gasperi, M. *et al*., 2002]. Cheung and Boyages , found thyroid enlargement by ultrasonography in 92% of 37 acromegaly patients, with a higher incidence of nodular disease in long-term acromegaly. They also found that individuals who were adequately treated for acromegaly (normal serum IGF-I levels) had smaller thyroid glands than those who had active acromegaly, implying that goiter may be partially reversible with control of disease. This was confirmed when treatment with Octereotide for 1 year resulted in reduction in thyroid size. [Cheung, N. W. *et al*., 1997]. There was a good relationship between thyroid size, and IGF–1 level in our study. This association was also recognized by Miyakawa, *et al*., (1988), who proposed that the development of goiter in acromegaly may be due to elevated levels of IGF-I. In vitro, IGF-I is one of the primary growth factors for FRTL-5 rat thyroid cells. The DNA synthesis in FRTL-5 cells was stimulated by serum from patients with acromegaly, and the serum IGF-I concentration correlated significantly with the ability of that serum to stimulate thymidine incorporation into the DNA of FRTL-5 cells (Tramontano, *et al*., 1986; Takahashi, *et al*., 1990). GH is another possibility for thyroid growth stimulation. The plasma GH level in our acromegalic patients was directly proportional to thyroid volume, mainly after 6 months' treatment which is significant. Ching *et al*., studied the effects of GH and TSH on goiter formation in rats, indicating that GH activity is mediated by IGF-I synthesis with evident relationship between plasma IGF-I levels and thyroid volume in acromegaly [Ching, M. C. H. *et al*., 1975]. In our study, patients with thyroid disorders tended to be older, demonstrating that the prevalence of goiter progressively increased with age, and we observed that in acromegalic patients, no influence of gender could be demonstrated in the development of thyroid disorders, at variance with the observation of a higher prevalence of goiter in males than females. Figure 3 shows the association between thyroid size and estimated duration of disease. This observation indicated an incremental increase in active disease duration in patients with homogeneous, heterogeneous, and nodular glands. Thyroid cells' intrinsic heterogeneity results in uneven growth after extended exposure to high doses of IGF-I . Cells with the highest intrinsic growth potential respond the most to IGF-I and produce daughter clones with comparable growth properties, eventually leading to nodule formation and autonomy. This is identical to any other chronic thyroid stimulation procedure in which nodularity is the end result, regardless of etiology (Studer, *et al*., 1989).

CONCLUSION

Thyroid gland size correlating with IGF-1 level and GH after three and six months of follow-up of a sample of acromegalic patients on monthly injection of Octereotide LAR 20 mg. This study confirms that goiter is a common finding in acromgaly, our findings suggest that early in the course of the disease, diffuse goiter occurs. With control of GH hypersecretion and subsequently IGF-1, a reduction in thyroid size occurs, so conversely we can have deduced acromgalic activity from thyroid volume and may be considered an additional useful peripheral parameter for rapid assessment of the activity of acromegaly and strongly recommended periodic thyroid evaluation by ultrasound in patient with acromegaly.

The Ethical Statement

The paper reflects the authors' own research and analysis in a truthful and complete manner. There is no Conflict of interest for this work.

REFERENCES

1. Melmed, S. "Acromegaly." *The New England Journal of Medicine*, 322.14 (1990): 966–977.
2. Wuster, C., Steger, S., Schmelzle, G., Gottswinter, A., Minne, J. H. W. & Ziegler, R. "Increased incidence of euthyroid and hyperthyroid goitres independently of thyrotropin in patients with acromegaly." *Hormone and Metabolism Research*, 23 (1991): 131–134.
3. Cannavò, S., Squadrito, S., Finocchiaro, M. D., Curtò, L., Almoto, B., Vieni, A. & Trimarchi, F. "Goiter and Impairment of Thyroid Function in Acromegalic Patients: Basal Evaluation and Follow-Up." *Hormone*

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and Metabolism Research, 32.5 (2000): 190–195.
4. Al Dallal, S. "Acromegaly: a challenging condition to diagnose." *International Journal of General Medicine*, 11 (2018): 337–343.
5. Banerjee, A., Patel, K. & Wren, A. M. "Acromegaly- clinical manifestations and diagnosis." *Pharmaceutical Journal*, 13 (2003): 273–278.
6. Gloria, L., Lara, P. & Fernando, C. "Clinical Manifestations and Diagnosis of Acromegaly." *International Journal of Endocrinology*, 2012 (2012).
7. Holdaway, I. M., Rajasoorya, R.C. & Gamble, G. D. "Factors influencing mortality in acromegaly." Journal of Clinical Endocrinology and Metabolism, 89.2 (2004): 667–674.
8. Isidro, M. L., Iglesias, P. D., Matias-Guiu, X. & Cordido, F. "Acromegaly due to a growth hormone-releasing hormone-secreting intracranial gangliocytoma." *Journal of Endocrinological Investigation*, 28.2 (2005): 162–165.
9. Laszlo, H., Hans, P., Lars, R. P., Jesper, R. A., Birger, H., Peter, S., Gorm, J. & Jens, M. H. "The Determination of Thyroid Volume by Ultrasound and Its Relationship to Body Weight, Age, and Sex in Normal Subjects." *The Journal of Clinical Endocrinology & Metabolism*, 56.2 (1983): 260–263.
10. William, D. M. & Alfred, B. K. "Ultrasound: The Requisites, Second Edition." *Mosby;* December 31, (2003).
11. Lucas, K. J. "Use of thyroid ultrasound volume in calculating radioactive iodine dose in hyperthyroidism." *Thyroid*, 10.2 (2000): 151–155.
12. Gasperi, M., Martino, E., Manetti, L., Arosio, M., Porretti, S., Faglia, G, *et al*. "Prevalence of thyroid diseases in patients with acromegaly: results of an Italian multi-center study." *Journal of Endocrinological Investigation*, 25.3 (2002): 240–245.
13. Cheung, N. W. & Boyages, S. C. "The thyroid gland in acromegaly: an ultrasonographic study." *Clin. Endocrinol. (Oxf.)* 46.5 (1997): 545-549.
14. Miyakawa, M., Saji, M., Tsushima, T., Wakai, K. & Shizume, K. "Thyroid volume and serum thyroglobulin levels in patients with acromegaly: correlation with plasma insulin-like growth factor I levels." Journal of Clinical Endocrinology and Metabolism 697 (1998): 973–978.
15. Tramontano, D., Cushing, G. W., Moses, A. C. & Ingbar, S. H. "Insulin-like growth Factor-I stimulates the growth of rat thyroid cells in culture and synergizes the stimulation of DNA synthesis induced by TSH and Graves'-IgG." *Endocrinology* 119.2 (1986): 940–942.
16. Takahashi, S., Conti, M. & Van Wyk, J. J. "Thyrotropin potentiation of insulin-like growth Factor-I dependent deoxyribonucleic acid synthesis in FRTL-5 cells: Mediation by an autocrine amplification factor(s)." *Endocrinology*, 126(1990): 736–745.
17. Ching, M. C. H., Schalch, D. S. & Lebda, N. J. A. "Role of growth hormone in the enhancement of the propylthiouracil-induced goitrogenesis by small doses of thyroxine." *Acta Endocrinol (Copenh)*, 79(1975): 238.
18. Studer, H., Peter, H. J. & Gerber, H. "Natural heterogeneity of thyroid cells: the basis for understanding thyroid function and nodular goitre growth." *Endocrine Reviews*, 10(1989): 125–135.

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