Original Article

Thyrotropin receptor antibodies measured by second-generation assay are highly specific for Graves' disease and correlate with serum thyrotropin levels in patients with Graves' disease in remission and during maintenance therapy

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Abstract

We compared conventional first-generation thyrotropin receptor antibodies（F-TRAb）and second-generation TRAb（S-TRAb, DYNOtest）in sera. Subjects were 167 cases of Graves' disease, 5 cases of painless thyroiditis, 8 cases of subacute thyroiditis, 37 cases of chronic thyroiditis, 19 cases of miscellaneous thyroid diseases, 36 cases of Type 1 diabetes mellitus, and 12 cases of other diseases. The latter 3 groups were all negative for thyroid autoantibodies. S-TRAb was completely negative in diseases other than Graves' disease except in 3 cases（8%）of chronic thyroiditis. In patients with Graves' disease overall, S-TRAb was positive in 102 cases（61%）and F-TRAb was positive in 72 cases（43%）; a positive correlation between S-TRAb and F-TRAb levels was noted. Fourteen cases of untreated Graves' disease were positive with both methods of measurement in all cases. In 52 cases of Graves' disease in remission and during maintenance therapy, F-TRAb was positive in only 1 case（2%）; S-TRAb was positive in 12 cases（23%）. Comparison with these 52 cases - 12 cases that were S-TRAb positive and 40 that were negative - indicated that in positive cases serum thyrotropin levels were significantly lower and serum free thyroxine significantly higher. In these 52 cases, a negative correlation between serum thyrotropin and S-TRAb levels was noted in addition to a negative correlation between serum thyrotropin and free thyroxine levels. In conclusion, S-TRAb is highly specific for Graves' disease except a few cases of chronic thyroiditis. In patients with Graves' disease in remission and during maintenance therapy, S-TRAb-positive cases are often noted in F-TRAb-negative cases. Since these S-TRAb-positive cases displayed a lower thyrotropin level and a higher free thyroxine level and there was a negative correlation between serum thyrotropin and S-TRAb levels, S-TRAb positivity may reflect minimal disease activity. Further analysis is necessary to examine a relationship between S-TRAb positivity and recurrence of Graves' disease after discontinuation of an antithyroid drug.

（Keywords: Graves' disease, chronic thyroiditis, thyrotropin receptor antibody, thyrotropin,

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thyroxine）

I. Introduction

Thyrotropin receptor antibodies（TRAb）are considered to be a principal cause of Graves' disease[1]. Measurement of TRAb is widely used in diagnosis of Graves' disease and follow-up with antithyroid drug therapy. A radioreceptor assay, which measures binding inhibition of bovine iodo-thyrotropin（TSH）and solubilized porcine TSH receptors, is widely used in current measurement of TRAb[2]. This method involves problems such as false negatives for Graves' disease, false positives for diseases other than Graves' disease, and uncertain significance at low concentrations[3-5]. Recently, a method of measurement using solid-phase human recombinant TSH receptors has been developed as a second-generation method of high-sensitivity TRAb measurement[6]. The present study was therefore undertaken to test the specificity of this high-sensitivity TRAb measurement for Graves' disease and its significance in patients with Graves' disease in remission and during maintenance therapy, particularly focusing on its relationship to disease activity.

II. Materials and Methods

A. Subjects

Subjects were a total of 284 cases（Table 1）including 167 cases of Graves' disease, 5 cases of painless thyroiditis, 8 cases of subacute thyroiditis, 37 cases of chronic thyroiditis, 19 cases of miscellaneous thyroid diseases（15 cases of adenomatous goiter, 2 cases of a thyroid cyst, and 2 cases of cretinism）, 36 cases of Type 1 diabetes mellitus, and 12 cases of other diseases（7 cases of Type 2 diabetes mellitus, 2 cases of hyperlipidemia, 2 cases of an eating disorder, and 1 case of simple obesity）. Subjects in the latter 3 groups were all negative for anti-thyroglobulin antibody（TgAb）and anti-thyroperoxidase antibody（TPOAb）. Informed consent was obtained for the use of sera to measure thyroid-associated antibodies as described below.

Graves' disease was, in addition to hyperthyroidism and the presence of a goiter, diagnosed by posi-

Table1 Overall characteristics of the subjects

	number (male：female)	age (years)	age at onset (years)	S-TRAb* positive（%）	F-TRAb** positive/number（%）
Graves' disease	167 (40：127)	48±15	43±15	102 (61%)	72/167 (43%)
Painless thyroiditis	5 (1：4)	31±11		0 (0%)	0/4 (0%)
Subacute thyroiditis	8 (0：8)	50±10		0 (0%)	0/8 (0%)
Chronic thyroiditis	37 (3：34)	49±16		3 (8%)	1/12 (8%)
Miscellaneous thyroid diseases***	19 (4：15)	43±13		0 (0%)	0/11 (0%)
Type 1 diabetes mellitus***	36 (18：18)	43±16	30±15	0 (0%)	not measured
Others***	12 (6：6)	46±18		0 (0%)	0/1 (0%)

Mean ± SD are shown.

* S-TRAb denotes second-generation thyrotropin receptor antibody. S-TRAb was measured in all cases.

** F-TRAb denotes first-generation thyrotropin receptor antibody. F-TRAb was not measured in all cases.

*** Thyroid autoantibodies（TgAb and TPOAb）were negative.

tivity of conventional first generation TRAb (TRAb [Cosmic] III, Cosmic Corporation, Tokyo) and/or increased uptake of ^{123}I into the thyroid gland determined by a ^{123}I thyroid scintigram at the time of initial presentation. Patients with Graves' disease were divided into three groups of 14 untreated cases; 52 cases in remission (n=9, no medication for the past half year or longer) and during maintenance therapy (administered less than 50 mg/day propylthiouracil or 5 mg/day methimazole with serum TSH level remaining in normal ranges for the past half year or longer); and 101 other cases principally treated with dosages above the maintenance dose. Patients in remission and during maintenance therapy did not include individuals with a history of isotope therapy and individuals receiving combined therapy with antithyroid drugs and levothyroxine.

Painless thyroiditis was, in addition to transient thyrotoxicosis, diagnosed by the presence of TgAb and/or TPOAb and decreased uptake of ^{123}I into the thyroid determined by a ^{123}I thyroid scintigram. Subacute thyroiditis was, in addition to transient thyrotoxicosis, diagnosed by the presence of a painful goiter, inflammatory response in sera (C-reactive protein-positive), and typical clinical course. Chronic thyroiditis was diagnosed by the presence of a diffuse goiter and positive TgAb and/or TPOAb.

B. Measurement

Levels of serum TSH, free triiodothyroine (free T3), and free thyroxine (free T4) were measured by ELISA kits (Tosoh Corporation, Tokyo, Japan). TgAb and TPOAb concentrations were measured by RIA kits (DYNOtest anti TG and DYNOtest anti TPO, Brahms Diagnostica, Berlin, Germany). DYNOtest TRAb Human "Yamasa" (Yamasa, Tokyo, Japan) was employed for second-generation measurement of TRAb (S-TRAb). The criterion for positivity was set to >1.5 IU/L, based on the recommendation (values exceeding reference values for a healthy individual) of Brahms Diagnostica, the kits' manufacturer[6]. This criterion is also widely used in other previous studies involving Japanese population[7-12]. In patients with Graves' disease, TRAb was also measured with a conventional first-generation method (TRAb [Cosmic] III Kit, Cosmic Corporation, Tokyo) (F-TRAb) at the SRL laboratory (Tokyo, Japan). The criterion for positivity was set to the SRL's criterion (>15%). Thyroid hormones, TgAb, TPOAb, S-TRAb, and F-TRAb were measured using serum taken at the same time. F-TRAb was also determined in 36 (31%) out of the 117 cases without Graves' disease,

With regard to 2 cases of chronic thyroiditis patients in whom S-TRAb was strongly positive, thyroid-stimulating antibody (TSAb) and blocking-type TSH receptor antibody (TSBAb) were also measured[13] using the same serum.

C. Statistical Analysis

Results are expressed as mean ± SD. Simple correlation was used to examine correlation. The Mann-Whitney U test or Fisher's exact probability were used to compare the two groups. These analyses were performed using the statistical package StatView 4.5 for Macintosh (Abacus Concepts, Berkeley, CA). A P value of less than 0.05 was considered significant.

III. Results

A. S-TRAb levels for various diseases

Diseases other than Graves' disease were all negative for S-TRAb except for 3 cases (8%) of chronic thyroiditis (Table 1). Among the 3 cases of chronic thyroiditis that were positive for S-TRAb, a single patient displayed a weakly positive concentration of S-TRAb (1.7 IU/L). The clinical characteristics of the

Table2 Clinical characteristics of 2 female patients with chronic thyroiditis and high levels of S-TRAb*

age (years)	TPOAb (U/ml)	TgAb (U/ml)	S-TRAb* (IU/l)	F-TRAb** (%)	TSAb (%)	TSBAb (%)	TSH (μu/ml)	free T4 (ng/dl)
40	52.5	1.7	17.6	not measured	995	48	1.97	1.13
66	11.8	1.9	15.0	53.4	132	65	0.02***	2.06***
Normal range	≦0.3	≦0.3	＜1.5	≦15.0	＜180	＜45	0.5-3.3	0.8-1.4

* S-TRAb denotes second-generation thyrotropin receptor antibody.

** F-TRAb denotes first-generation thyrotropin receptor antibody.

*** These values were obtained while the patient taking levothyroxine 100 μg/day.

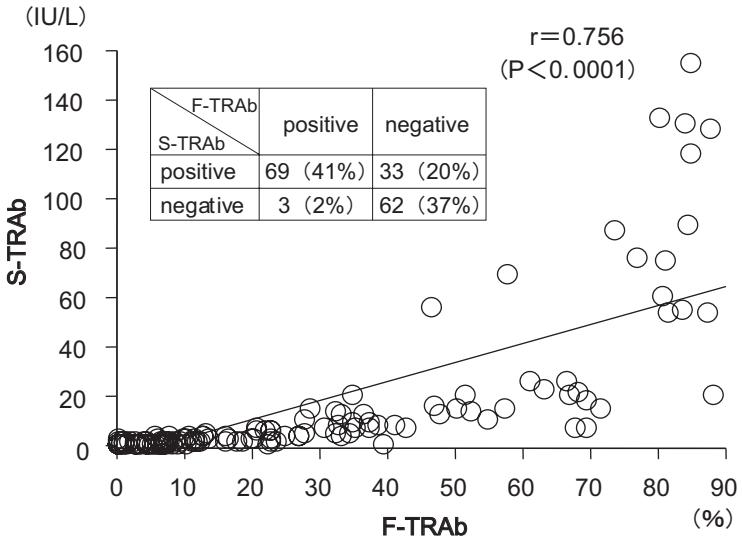

Fig.1：Correlation between first-generation (F-TRAb) and second-generation (S-TRAb) TSH receptor antibody levels in patients with Graves' disease (n=167).

remaining 2 cases with high concentrations of S-TRAb were shown in Table 2. The subjects were TSAb or TSBAb-positive. In the TSB-Ab-positive patient who underwent F-TRAb measurement, F-TRAb was also positive, and levothyroxine had been administered for the treatment of hypothyroidism. F-TRAb was negative in all other cases with painless thyroiditis, subacute thyroiditis, miscellaneous thyroid diseases and other diseases who underwent the measurement (Table 1).

B. Studies in Graves' disease

There was a positive correlation between S-TRAb and F-TRAb in the 167 cases of Graves' disease (Fig. 1). In Graves' disease overall, S-TRAb was positive in 102 cases (61%) and F-TRAb was positive in 72 cases (43%). As shown in Fig.1, most of the F-TRAb-positive cases were also positive for S-TRAb, although a few exceptional cases were also found. About one third of the F-TRAb-negative cases were positive for S-TRAb.

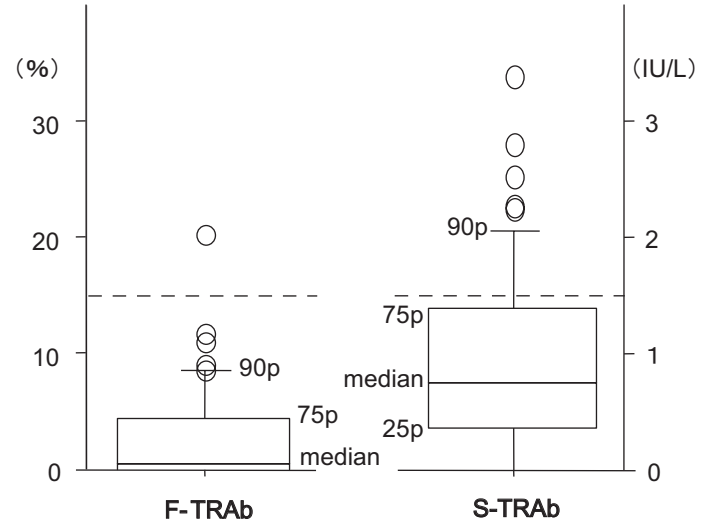

Fig.2：First-generation（F-TRAb）and second-generation（S-TRAb）TSH receptor antibody levels in patients with Graves' disease in remission and during maintenance therapy（n=52）. With the former, 1 case（2%）was positive; with the latter, 12 cases（23%）were positive. The dotted line indicates the criterion for positivity. The box denotes 25~75 percentile of the levels（25p and 75p, respectively）, and 90 percentile of the levels（90p）is also shown. Each circle denotes an individual level exceeding 90 percentile of the levels.

In 14 cases of untreated Graves' disease, all cases were positive with both methods of measurement. In 52 cases of Graves' disease in remission and during maintenance therapy, F-TRAb was positive in only 1 case（2%）, whereas S-TRAb was positive in 12 cases（23%）(Fig. 2). In the remaining 101 cases principally being treated with dosages above the maintenance dose, F-TRAb was positive in 57 cases（56%）, and S-TRAb was positive in 76 cases（75%）.

With regard to the 52 cases of Graves' disease in remission and during maintenance therapy, 12 cases were S-TRAb positive and the remaining 40 were negative（Table 3）. In both groups, there was no difference in sex, age, age at onset, duration of the disease, proportion of subjects in remission, and levels of TPOAb, TgAb, and free T3. Among the subjects during maintenance therapy, there was no difference in the frequency of methimazole or propylthiouracil use as well as in the dose of the drugs. In S-TRAb-positive cases, serum TSH levels were significantly lower and serum free T4 levels were significantly higher as compared to the negative cases. F-TRAb levels were also higher in positive cases, although those were almost within normal ranges（Fig. 2）.

In these 52 cases, a negative correlation between serum TSH and free T4 levels was noted（Fig. 3）; in addition, a negative correlation between serum TSH and S-TRAb levels was also noted. There was no correlation between serum TSH and F-TRAb levels. Both S-TRAb and F-TRAb levels were not associated with serum free T4 levels（data not shown）.

Table3 Comparison of patients with Graves' disease in remission and during maintenance therapy according to S-TRAb* positivity

	S-TRAb* positive	S-TRAb* negative	P value**
number (male ; female)	12 (4 ; 8)	40 (6 ; 34)	0.213
age (years)	50 ± 20	50 ± 15	0.811
age at onset (years)	42 ± 16	42 ± 15	0.862
duration (years)	8 ± 7	9 ± 6	0.556
in remmision (n)	2	7	0.660
maintenance therapy (n)	10	33	
methimazole (n) (dose)	9 (4.7 ± 0.8 mg/day)	23 (3.8 ± 1.3 mg/day)	0.195
propylthiouracil (n) (dose)	1 (50 mg/day)	10 (45 ± 17.5 mg/day)	
TPOAb (U/ml)	68 ± 132	25 ± 44	0.409
TgAb (U/ml)	6.7 ± 12.1	8.9 ± 34.3	0.307
TSH (μU/ml)	1.6 ± 1.3	2.7 ± 1.7	0.035
free T3 (pg/ml)	2.3 ± 0.2	2.2 ± 0.3	0.561
free T4 (ng/dl)	1.1 ± 0.1	1.0 ± 0.2	0.044
F-TRAb*** (%)	6.5 ± 5.9	1.6 ± 2.5	0.001

Mean ± SD. * S-TRAb denotes second-generation thyrotropin receptor antibody.

** P value is calculated by Mann-Whitney U test or Fisher's exact probability (category data).

*** F-TRAB denotes first-generation thyrotropin receptor antibody.

IV. Discussion

TRAb measurement is widely used clinically in diagnosis and management of Graves' disease. There are several problems with this method including false negatives for Graves' disease, false positives for diseases other than Graves' disease, and recurrence of Graves' disease after discontinuation of an antithyroid drug in cases displaying negative TRAb levels during the course of therapy[3-5, 14, 15]. The present study examined some of these problems using a second-generation method of measurement using human recombinant TSH receptors.

In the present study, diseases other than Graves' disease were all negative for S-TRAb except for 3 cases (8%) that were clinically diagnosed as chronic thyroiditis. In patients with Type 1 diabetes mellitus, which is often accompanied with autoimmune thyroid disorders, as well as miscellaneous thyroid diseases, S-TRAb was all negative. Measurement with S-TRAb was therefore highly specific for Graves' disease, which coincides with past reports[6-12, 16, 17]. When TSAb and TSBAb were examined with regard to the 2 cases of chronic thyroiditis with high levels of S-TRAb, either was positive. One TSAb-positive case had normal thyroid function at the current time, although this thyroid function may vary in the future. One TSBAb-positive case was receiving thyroxine replacement due to hypothyroidism that may be caused by TSBAb. This case was also positive for F-TRAb. Since S-TRAb as well as F-TRAb is determined by using principles of radioreceptor assay[6], the functional properties of TRAb cannot be clarified. The results in positive cases must be interpreted in comparison to the clinical picture.

In all patients with untreated Graves' disease, TRAb was positive with both methods of measurement, although in cases treated with dosages above the maintenance dose F-TRAb was positive in 56%, and

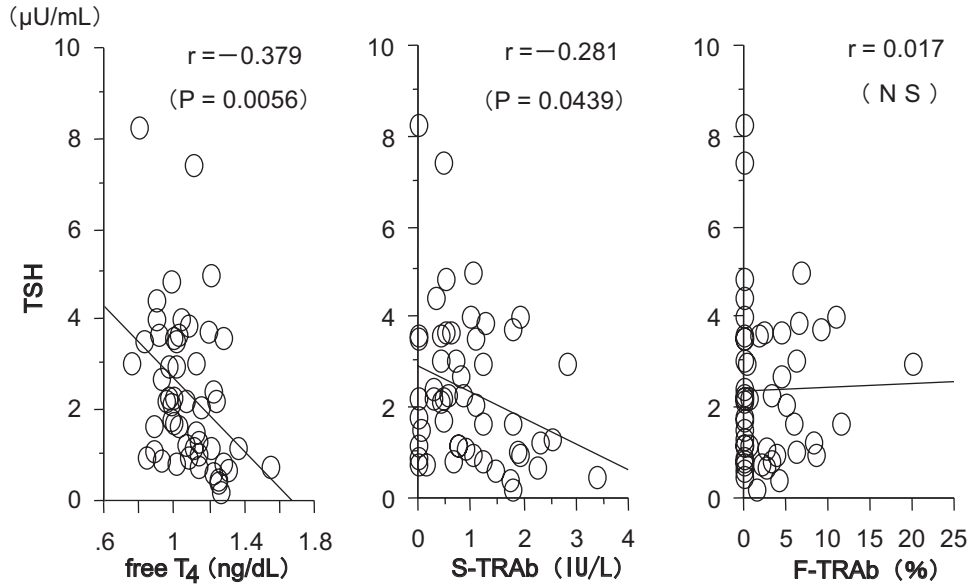

Fig.3：Correlation between serum free T4, second-generation（S-TRAb）and first-generation（F-TRAb）TSH receptor antibody, and serum TSH levels in Graves' disease patients in remission and during maintenance therapy（n=52）.

S-TRAb was positive in 75%; the positive rate with S-TRAb was higher. In patients with Graves' disease in remission and during maintenance therapy with low doses of antithyroid drug, F-TRAb was negative in almost all cases, although S-TRAb was positive in 23%, and the largest difference in the positive rate was noted in this subgroup.

To examine the implication of S-TRAb positivity for Graves' disease in remission and during maintenance therapy, 12 positive cases and 40 negative cases were compared. A difference in age, duration of the disease, and levels of TgAb and TPOAb was not noted between the 2 groups, although in positive cases serum TSH levels were significantly lower and serum free T4 levels were higher. Furthermore, a negative correlation between serum TSH and S-TRAb levels was demonstrated, in addition to a negative correlation between serum TSH and free T4 levels. S-TRAb positivity may therefore suggest greater residual activity of Graves' disease, even though the serum levels of TSH and free T4 were almost within normal ranges. TRAb per se is also reported to suppress TSH secretion[18], and the present results are in accordance with this observation. In contrast, a correlation between serum TSH and F-TRAb levels was not noted. It seems likely that F-TRAb lacks enough quantitative sensitivity in this range of almost normal thyroid function.

In patients with Graves' disease during maintenance therapy with an antithyroid drug, F-TRAb negativity is considered to be a prerequisite for discontinuation of medication although it is not sufficient to guarantee successful discontinuation[14, 15]. In the present study, there were a number of S-TRAb-positive cases even among such F-TRAb-negative patients, and in these cases the residual activity of Graves' disease might be greater as discussed above. Therefore, S-TRAb may provide more accurate information for the necessity of continuing an antithyroid drug. With regard to this point, Maugendre et al.[19] reported that

S-TRAb could serve as a predictor of relapse of Graves' disease in a short period of time, although there is also a contradictory report[20]. Schott et al.[21] recently disclosed that relapse of Graves' disease could be better predicted by the combined measurement of S-TRAb and TPOAb. Further analysis is necessary to examine a relationship between S-TRAb positivity and recurrence of Graves' disease after discontinuation of an antithyroid drug in Japanese patients with Graves' disease.

In the present study, F-TRAb measurement is based on the assay using porcine TSH receptors and polyethylene glycol precipitation method[2], and S-TRAb is on the assay using human TSH receptors and coated-tube method[6]. The higher positive rate of S-TRAb in patients with Graves' disease is likely due to the coated-tube method rather than different TSH receptors used, because the same positive rate is observed by the coated-tube measurement using human or porcine TSH receptors[12, 22, 23].

In conclusion, S-TRAb is highly specific for Graves' disease, and positive cases are often noted in conventional F-TRAb-negative cases of Graves' disease in remission and during maintenance therapy. This S-TRAb positivity may reflect minimal disease activity, since these cases displayed a lower TSH level and a higher free T4 level, and there was a negative correlation between serum TSH and S-TRAb levels.

References

1) Zakarija M and McKenzie JM: The spectrum and significance of autoantibodies reacting with the thyrotropin receptor. Endocrinol Metab Clin North Am 16 : 343-363, 1987.
2) Smith BR and Hall R: Thyroid-stimulating immunoglobulins in Graves' disease. Lancet 2 : 427-431, 1974.
3) Ilicki A, Gamstedt A and Karlsson FA: Hyperthyroid Graves' disease without detectable thyrotropin receptor antibodies. J Clin Endocrinol Metab 74 : 1090-1094, 1992.
4) Kawai K, Tamai H, Matsubayashi S et al: A study of untreated Graves' patients with undetectable TSH binding inhibitor immunoglobulins and the effect of anti-thyroid drugs. Clin Endocrinol (Oxf) 43 : 551-556, 1995.
5) Morita T, Tamai H, Oshima A et al: The occurrence of thyrotropin binding-inhibiting immunoglobulins and thyroid-stimulating antibodies in patients with silent thyroiditis. J Clin Endocrinol Metab 71 : 1051-1055, 1990.
6) Costagliola S, Morgenthaler NG, Hoermann R et al: Second generation assay for thyrotropin receptor antibodies has superior diagnostic sensitivity for Graves' disease. J Clin Endocrinol Metab 84 : 90-97, 1999.
7) Yoshimura H, Hamada N, Shimizu T et al: Establishment of cut off value and clinical effect by TRAb measurement kit using human recombinant TSH receptor. Jpn J Med Pharm Sci 47 : 127-133, 2002.
8) Fukata S, Kubota S, Hiraiwa T et al: Differentiation of TRAb negative Graves' disease from silent thyroiditis using DYNOtest TRAb human kit "YAMASA". Jpn J Med Pharm Sci 47 : 311-315, 2002.
9) Anahara Y, Ikeda M, Takahashi K et al: Fundamental and clinical evaluations of thyrotropin receptor antibody assay using recombinant human thyrotropin receptors. Jpn J Med Pharm Sci 49 : 293-299, 2003.
10) Ban Y, Ban Y, Nagata A et al: Evaluation of diagnostic efficacy on TRAb-human kit for Graves' diseases. Jpn J Med Pharm Sci 50 : 199-203, 2003.
11) Tagami T, Usui K, Shimazu A et al: Studies on the clinical application of TSH binding inhibitor im-

munoglobulin measurement using the second-generation assay for thyrotropin receptor antibodies. Clin Endocrinol（Tokyo）51 : 387-394, 2003.

12）Kamijo K: TSH-receptor antibody measurement in patients with various thyrotoxicosis and Hashimoto' s thyroiditis: a comparison of two two-step assays, coated plate ELISA using porcine TSH-receptor and coated tube radioassay using human recombinant TSH-receptor. Endocr J 50 : 113-116, 2003.

13）Kasagi K, Nagata A, Yoshimura H et al: Studies on the clinical application of TSBAb measurement using TSAb kit "Yamasa". Clin Endocrinol（Tokyo）46 : 913-924, 1998.

14）Kasagi K, Iida Y, Hatabu H et al: Evaluation of TSH-receptor antibodies as prognostic markers after cessation of antithyroid drug treatment in patients with Graves' disease. Acta Endocrinol（Copenh）117 : 173-180, 1988.

15）Feldt-Rasmussen U, Schleusener H and Carayon P: Meta-analysis evaluation of the impact of thyrotropin receptor antibodies on long term remission after medical therapy of Graves' disease. J Clin Endocrinol Metab 78 : 98-102, 1994.

16）Komori A, Jibiki K, Yamaguchi N et al: Fundamental and clinical studies of thyrotropin binding inhibition assay by recombinant human thyrotropin receptors. Jpn J Med Pharm Sci 46 : 563-570, 2001.

17）Mankai A, Toumi D, Chadli-Chaieb M et al: Anti-thyroid-stimulating hormone receptor antibodies determined by second-generation assay. Clin Chem Lab Med 45 : 26-29, 2007.

18）Brokken LJ, Wiersinga WM and Prummel MF: Thyrotropin receptor autoantibodies are associated with continued thyrotropin suppression in treated euthyroid Graves' disease patients. J Clin Endocrinol Metab 88 : 4135-4138, 2003.

19）Maugendre D and Massart C: Clinical value of a new TSH binding inhibitory activity assay using human TSH receptors in the follow-up of antithyroid drug treated Graves' disease. Comparison with thyroid stimulating antibody bioassay. Clin Endocrinol（Oxf）54 : 89-96, 2001.

20）Zimmerman-Belsing T, Nygaard B, Rasmussen AK et al: Use of the 2nd generation TRAK human assay did not improve prediction of relapse after antithyroid medical therapy of Graves' disease. Eur J Endocrinol 146 : 173-177, 2002.

21）Schott M, Eckstein A, Willenberg HS et al: Improved prediction of relapse of Graves' thyrotoxicosis by combined determination of TSH receptor and thyroperoxidase antibodies. Horm Metab Res 39 : 56-61, 2007.

22）Okamoto Y, Tanigawa S, Ishikawa K et al: TSH receptor antibody measurements and prediction of remission in Graves' disease patients treated with minimum maintenance doses of antithyroid drugs. Endocr J 53 : 467-472, 2006.

23）Zophel K and Wunderlich G: Predictive value of TSH receptor antibody measurement in Graves' disease is independent on the TSH receptor（human or porcine）but depends on the generation of the assay used. Endocr J 53 : 869-870, 2006.

第二世代 TSH 受容体抗体の臨床的検討

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要　約

第一世代 TSH 受容体抗体（F-TRAb）と第二世代（S-TRAb）を比較検討した。対象は Graves 病167例，無痛性甲状腺炎５例，亜急性甲状腺炎８例，慢性甲状腺炎37例など，合計284例。S-TRAb は Graves 病以外で，慢性甲状腺炎のうち３例で陽性であったが，その他ではすべて陰性であった。Graves 病全体では，S-TRAb 陽性は102例（61％），F-TRAb 陽性は72例（43％）であった。S-TRAb と F-TRAb の間には正相関を認めた。未治療 Graves 病14例は全例両測定法とも陽性だったが，緩解または維持療法中の52例では，S-TRAb 陽性は12例（23％），F-TRAb 陽性は１例（２％）で，陽性率に差を認めた。緩解または維持療法中の52例で，S-TRAb 陽性12例と陰性40例を比較すると，陽性例で TSH が低値，フリー T4が高値であった。またこれら52例では，S-TRAb，フリー T4と TSH の間に負の相関を認めたが，F-TRAb と TSH の間には相関を認めなかった。以上の結果から，S-TRAb は Graves 病に特異性が高く，また Graves 病緩解または維持療法中の症例では，疾患活動性を鋭敏に反映する可能性が示唆された。S-TRAb が，抗甲状腺薬の中止の指標になるかどうかは，今後の検討課題である。

（キーワード：Graves 病，慢性甲状腺炎，TSH 受容体抗体，TSH，T4）

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