A Study on Achiles Tendon Reflex in Normal Korean Persons and Various Thyroid Diseases

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Introduction

Since Chaney[1] reported the measurement of ankle jerk in Patients with myxedema for the first time, slowing of the reflex in myxedema has been well documented by many authors. Although its mechanisms have not been elucidated clearly, it has long been held in esteem by clinicians a near pathognomonic sign in myxedema. Possible mechanisms suggested include (a) abnormal activity of the central nervous system, (b) a disorder of muscle like that of myotonia[2] (c) lowered temperature of the muscle, (d) increased viscosity of themuscle due to myxdematous infiltration[3] and (e) part of a general slowing of all vital processes.

The brisk reflex in thyrotoxicosis has also been noted to be characteristic. The recent development of several simple methods of quantitating the deep tendon reflex time has made its application an easy, rapid, inexpensive and accurate test in the results of our examinations on the Achilles tendon reflex(ATR) times in normal Koreans along their sexes, ages and in various thyroid diseases. Also we observed the changes of ATR times in the thyrotoxicosis and myxedema after the initiation of treatment and compared them with other thyroid function tests.

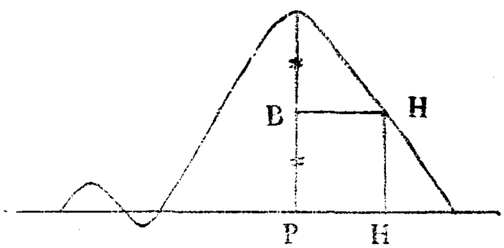

Fig. 1. Typical photomotogram tracing. Since the end of the relaxation phase does not have a sharp end-point, the time of one half relaxation is usually used(S—H). Contraction phase is from S to p (S—P).

Materials and Methods

The ATR times were recorded serially in 533 persons. Of these persons, 340 were normal Koreans (Male 190, Female 150.) who were proved to be normal through routine clinical examinations and 193 were various thyroid disease patients who visited the Department of Internal Medicine, College of Medicine, Seoul National University, from April 1975 through August 1977.

The group of various thyroid diseases included 89 hyperthyroid patients, 19 hypothyroid disease patients and 85 other thyorad disease patients (nontoxic diffuse goiter 42, nontoxic nodular goiter 35, thyroid cyst 8), who were euthyroid by criteria of various thyroid function tests. The diagnosis of hyperthyroidism or hypothyroidism was based on appraisals by physicians, supported by the results of thyroid function test which included radioactive iodine uptake(normal range 15—40%), T_3—resin uptake (normal range

23—32%), effective thyroxine ratio (normal range 0.86—1.13), and serum TSH by radioimmunoassay (normal range 2.5—6 micro-unit per ml). Effective thyroxine ratio(ETR) reflects both binding capacity of TBG and serum T_4 concentration, so that it can be serum free-thyroxine index(FTI.) We used Res —0 Mat ETR KIT of Mallinckrodt Co., USA for ETR determination and in the measurement of T_3 —resin uptake(T_3RU), Triosorb—125 KIT of Abbott Co., USA. The measurement of ATR time was made with patients in kneeling position with photomotograph*. The photomotograph consists of a light source and a photo-cell, so arranged that the foot casts a shadow on the photo-cell. Movement of the foot in the light beam generates a change in photo-cell voltage, and a record (photomotogram) is produced by an ordinary direct-writing electrocardiograph that gives a time-position plot of reflex action. (Fig. 1.) The peak of the curve recorded in the photomotogram is the end of contraction (maximum movement), and the point where the curve descends to the baseline is the end of relaxation.

Because the end of relaxation shows usually not

Table 1. Age & sex distribution of A.T.R.(S-H value) in normal control
Mean±S.D.(Unit;msec)

Age \ Sex	Male	Female
11—20	250±27(62) (200—320)	266±27(36) (200—320)
21—30	271±31(38) (220±380)	284±27(21) (240—360)
31—40	273±25(26) (240—320)	291±27(29) (220—350)
41—50	286±35(20) (230—350)	307±42(24) (240—400)
51—60	296±33(20) (260—380)	318±46(20) (240—420)
61—	301±33(24) (240—330)	325±35(20) (270—400)
Total	272±35(190) (200—300)	295±41(150) (200—420)

* This apparatus was kindly donated by "Alexander von Humboldt Stiftung" (Bad Godesberg/Rh) in West Germany.

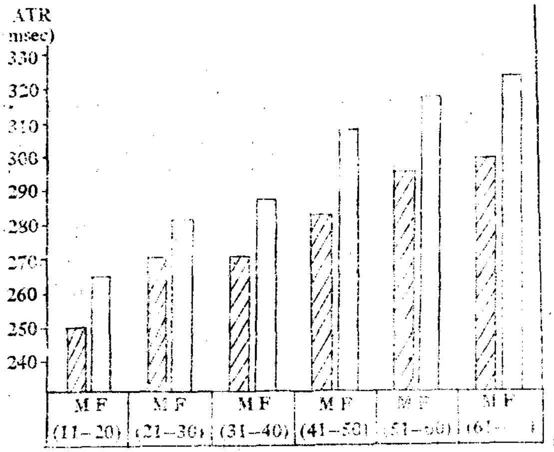

Fig. 2. Age and sex distribution of ATR in normal control.

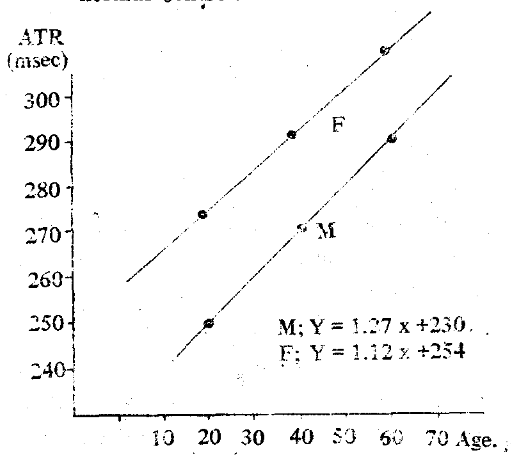

Fig. 3. The regression equation of ATR on age is Y=1.27X+230, Y=1.12X+254 in male and female, respectively. And the regression is proved to be linear.

a sharp endpoint, the time between the tap on the tendon and the movement when the muscle was halfway relaxed-"tap-to-one-half-relaxation time" (S-H)-was recorded. This was regarded as the "reflex time".

The tap-to-end-of-contraction time was also recorded. The electrocardiograph run at a speed of 25mm per second.

Results

Achilles Tendon Reflex (ATR) Times in Normal Koreans

Table 2. Age Distribution of Achilles Tendon Reflex Times in Various Thyroid Diseases and Normal Controls Mean±S.D. (unit; msec)

Ages	Normal Control	Hyperthyroidism	Euthyroidism	Hypothyroidism
21—30	284±27	229±22	282±21	480
31—40	297±27	222±19	296±39	420±79
41—50	307±42	221±13	290±17	397±66
51—60	318±46	233±22	316±23	414±61
61—	325±35	232±14	310±22	—
Total	295±41	221±20	287±33	414±65

Table 3. Laboratory Findings in Various Thyroid Diseases Mean±S.D.

	ETR	T_3RU(%)	R.A.I. Uptake (%)	TSH micro unit/ml	ATR msec
Hyperthyroidism	1.24±0.10	48.7±7.7	67.4±16.8	—	221±20
Euthyroidism	1.00±0.07	28.9±4.2	34.9±1.47	—	287±33
Normal Control	0.86—1.13	23—32	15—45	0—8	295±41
Hypothyroidism	0.87±0.06	24.0±3.0	—	67±35	414±65

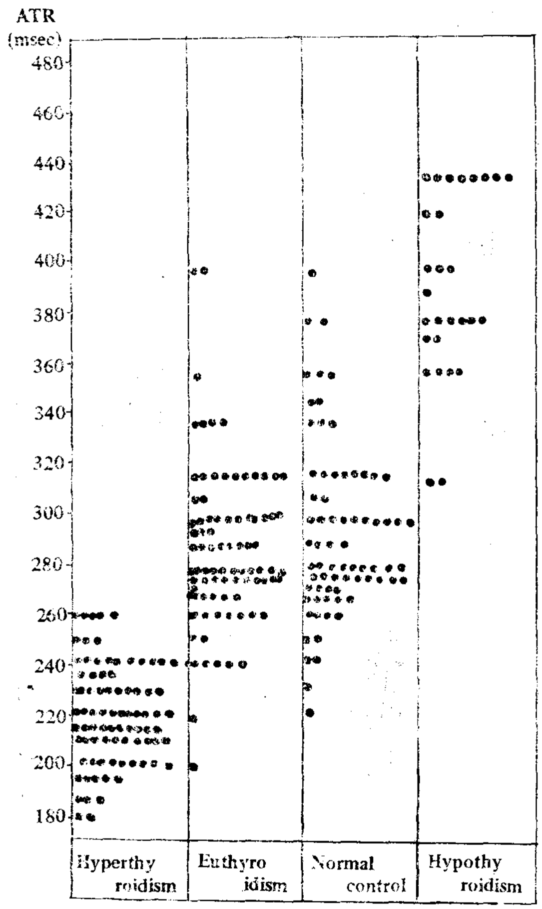

Fig. 4. ATR in various thyroid diseases.

ATR times in normal Korean persons were shown in Table 1 and Fig. 2 and revealed difference along their ages and sexes.

In male, mean ATR times along ages increased from their second decade with 250±27msec to 271 ±27msec in the third decade.

Thereafter ATR times increased progressively with ages in the 5th decade, 286±25msec and over 7th decade, 301±33msec.

Almost same trend was noticed in the female group, with mean ATR time of 266±27msec in the second decade and 325±35msec in over 7th decade of ages. The regression analysis of ATR time on age was proved to be linear, with a regression equation of Y=1.27X+230 and Y=1.12 X+254 in male and female, respectively. In the test for independence of ATR time on age, the t-values were 11.36 for male and 6.91 for female therefore, there was statistical significance between age groups. In comparison of the slopes, the t-value was 1.36, accordingly, the difference of ATR time increment between male and female seems to be of no statistical significance. And we also observed the reflex time is a little longer than in male, but it was not significant statistically.

Achilles Tendon Reflex Times in Various Thyroid Diseases (Table. 2, Table, 3, and Fig. 4.)

Mean ATR time in 89 hyperthyroidism patients was 221±20msec (180—260msec) and in comparison with that of normal controls (295±45msec), it was significantly shortened. ($p<0.01$).

Mean ATR time in 19 hypothyroidism patients was 414±65msec (320—520msec) and in comparison with that of normal controls, it was significantly delayed ($p<0.01$).

Mean ATR time in 85 other thyroid diseases (nontoxic diffuse goiter 42, nontoxic nodular goiter 35, thyroid cyst 8) was 290±36msec (210—400msec). Compared with that of normal controls, there was no significant difference statistically.

Contraction time(S—P) and half-relaxation time (P—H) of Achilles Tendon Reflex in normal controls and various thyroid disease patients(Table 4).

In normal controls, the mean contraction time was 176±22msec and the mean half-relaxation time was 118±33msec.

In hyperthyroidism, the mean contraction time was 154±14msec and the mean half-relaxation time was 68±14msec.

In hypothyroidism patients, the mean contraction time was 215±42msec and the mean half-relaxation time was 201±42msec.

We noted that the half-relaxation time was affected to the greatest extent in both hyperthyroidism and hypothyroidism.

We also noted that the contraction timewas affected considerably in both hyperthyroidism and hypothyroidism.

Accordingly we used the measurement from the start of initial stimulus to one half-relaxation time for the clinical purposes(S—H). This includes all of contraction phase(S—P) and approximately half of relaxation phase(P—H).

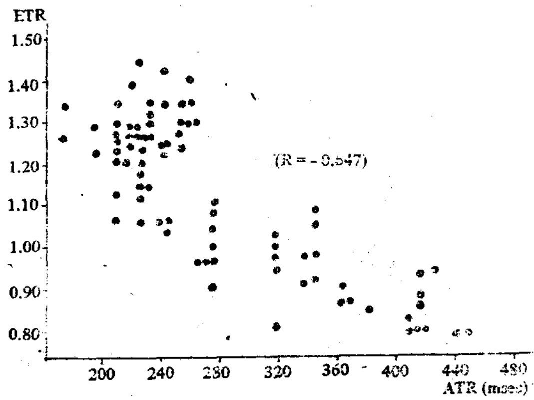

Fig. 5. Correlation between ETR and ATR.

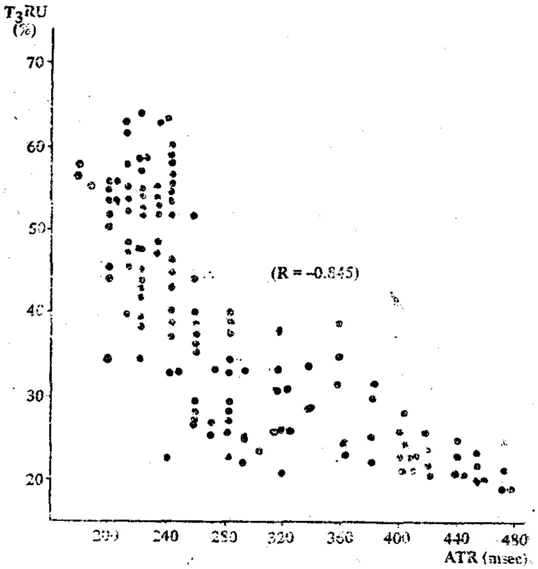

Fig. 6. Correlation between T_3RU and ATR.

Table 4. Comparison between S—H value and P—H value in various conditions

Mean±S.D. (unit;msec)

	Contraction time (S—P)	Half-relaxation time (P—H)	Contraction +Half relaxation time(S—H)
Normal	176±22	119±33	295±41
Hyperthyroidism	154±14	68±17	221±20
Hypothyroidism	213±42	201±49.4	414±65

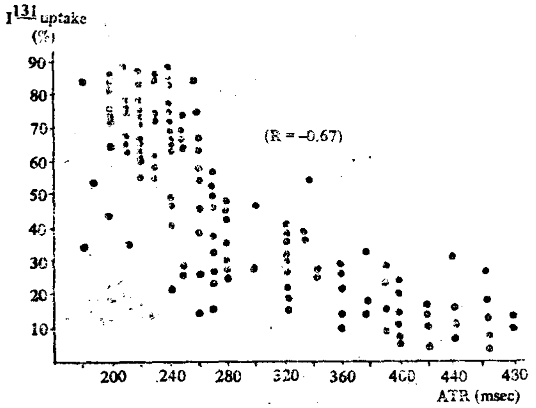

Fig. 7. Correlation between ^{131}I-uptake and ATR.

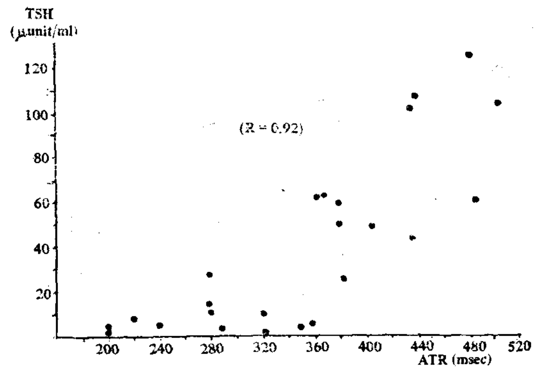

Fig. 8. Correlation between ATR and serum TSH level.

Comparison of Achilles Tendon Reflex (ATR) time with other tests for thyroid function.

Compared with the several other laboratory results, ATR time as a thyroid function test was evaluated.

ATR time showed the good correlation with effective thyroxine ratio (r=−0.6470), with 24 hour thyroidal radioactive iodine uptake (r=−0.67), with T_3 resinuptake value (r=−0.85) and serum immunoreactive TSH (r=−0.92), as shown in Fig. 5, 6, 7 and 8 respectively.

The Changes of Achilles Tendon Reflex times in various thyroid diseases after treatment.

1) Hyperthyroidism

We investigated serial changes of ATR times in 89 hyperthyroidism patients following treatment and compared them with their clinical courses and thyroid function tests which included ETR and T_3-resin uptake. (Table 5, and 6, Fig. 9 and 10).

We devided 89 hyperthyroidism patients into two groups at random, radioactive iodine (^{131}I) with antithyroid and antithyroid only groups as far as there was no contraindication in treatmeat.

The first group whch included 45 patients was treated with both ^{131}I and antithyroid (methimazole) simultaneously. After minimum doses of 4mCi of ^{131}I, we gave the patients 30-45mg of methimazole daily during the first several weeks of treatment. Dosage of methimazole decreased as their clinical conditions and thyroid function tests became improved and at last treated them with only maintenance dose(5-10mg) when they became euthyroid state. The mean of ATR time before treatment was 220±20 msec, but it became 258±26msec at the first month 285±28msec at the second month and 289±24msec at the third month

The changes of ATR time in the first and the

Table 5. ATR and TFT in Hyperthyroidism after Treatment with ^{131} I and Methimazole

Mean±S.D.

	Patient Number	ATR(msec)	ETR	T_3 RU(%)
Refore Treatment	45	220±20	1.25±0.10	50.7±7.7
1 month after Treatment	45	258±26	1.12±0.08	38.6±6.1
2 months after Treatment	45	285±28	1.04±0.07	31.1±4.6
3 months after Treatment	45	289±24	1.00±0.06	28.8±4.1

Table 6. ATR and TFT in Hypothyroidism after Treatment with Methimazole only

Mean±S.D.

	Patient Number	ATR(msec)	ETR	T_3 RU(%)
Before Treatment	44	221±20	1.23±0.10	46.8±7.6
1 month after Treatment	44	249±24	1.16±0.09	39.6±6.2
2 months after Treatment	44	268±25	1.10±0.07	33.6±5.2
3 months after Treatment	44	282±25	1.03±0.06	28.2±4.9

second month after treatment were significant statistically ($P<0.005$ $P<0.005$, respectively). And also in the third month ($P<0.05$). They were found to be euthyroid state clinically 2 months after treatment and at that time the values of ETR and T_3 RU were compatiale with

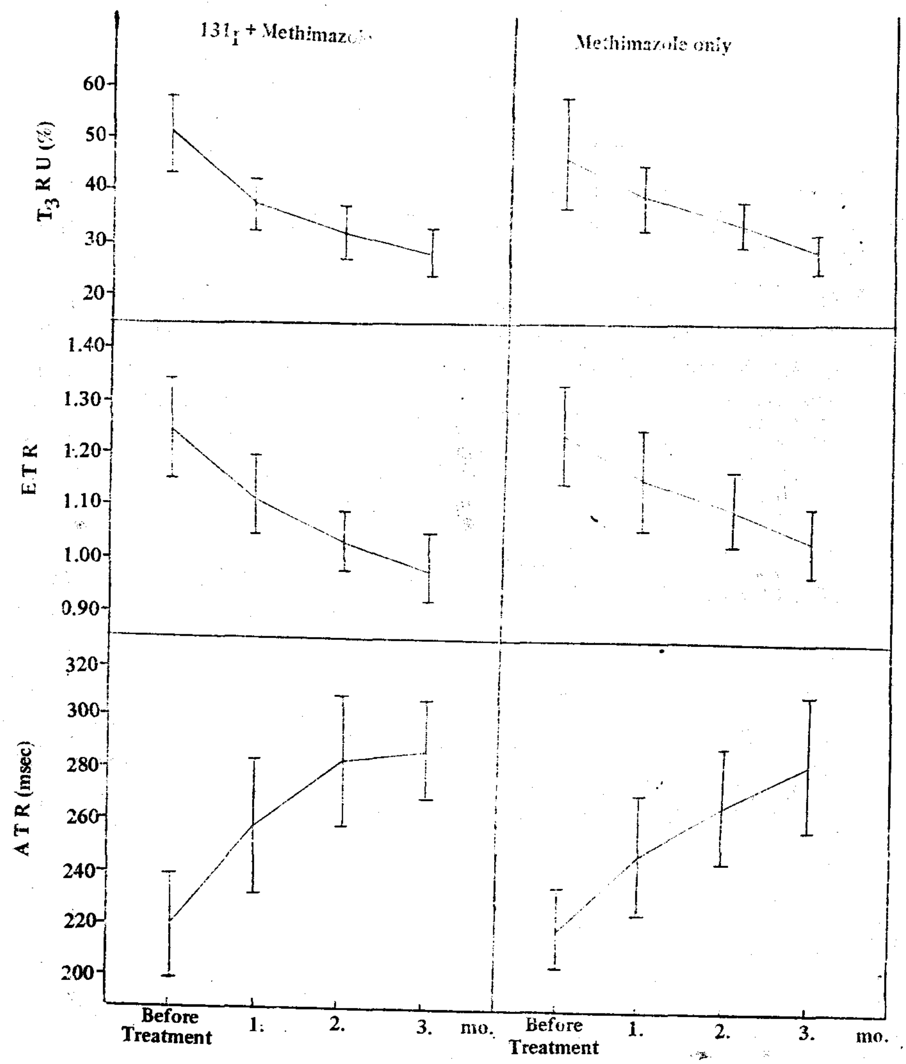

Fig. 9. Changes of ATR and TFT in Hyperthyroidism after Treatment.

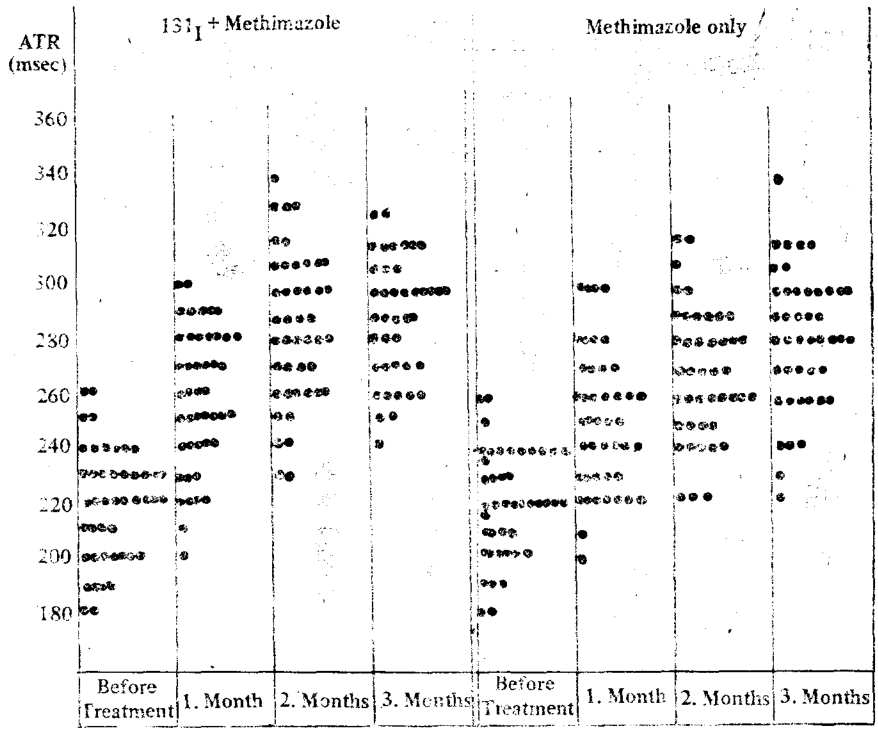

Fig. 10. Changes of ATR in Hyperthyroidism during Treatment.

euthyroid state and the mean of ATR times was not different statistically compared with that of normal controls($P>0.05$).

The second group included 44 patients who were treated with only methimazole. We used 30-45mg of methimazole during the first several weeks of treatment and we decreased the dosage as same way as in the first group. The mean ATR time before treatment in this group was 221 ± 20 msec and became $249\pm$msec 1 month after treatment, 268 ± 25msec 2 months and 285 ± 25msec 3 months.

The differences of ATR times of the first month after treatment and in second month from untreated state were statistically different with p-value of 0.005 in both. Also we realized that the changes of Achilles time were consistent with those of clinical courses and ETR and T_3RU. Furthermore we observed that the combined treatment with ^{131}I and methimazle was superior to that of methimazole only in the induction of hyperthyroidism into euthyroid state.

2) **Hypothyroidism**

Serial changes of ATR time were observed in 19 hypothyroidism patients following treatment and the results were compared with clinical courses and thyroid function tests which included ETR and T_3RU. (Table. 7, Fig. 11, and 12) Synthyroid (sodium levothroxine) was used for the treatment. In the first week, we used 50 microgram daily and added 25 micro-gram weekly and at last treated them with maintenance doseof 2.5 microgram/kg/day. The mean of ATR times before treatment was 414 ± 65msec but it became 330 ± 73 msec at 1 month and 289 ± 28msec at 2 month after treatment. The changes of ATR in the first month were statistically significant ($P<0.005$), and was same for the second month ($P<0.05$).

From clinical point of view, we could conclude that they became euthyroid state 2 month after treatment and also the values of their thyroid function tests were consistent with their clinical status. At that time the mean of their ATR times was in normal range.

Table 7. ATR and TFT in Hypothyroidism after Treatment with Synthyroid

Mean±S.D.

	Patient Number	ATR(msec)	ETR	T_3RU(%)
Before Treatment	19	414±65	0.87±0.06	24.0±3.0
1 month after Treatment	19	330±37	0.98±0.07	28.4±3.6
2 months after Treatment	19	289±28	1.02±0.07	30.5±4.3

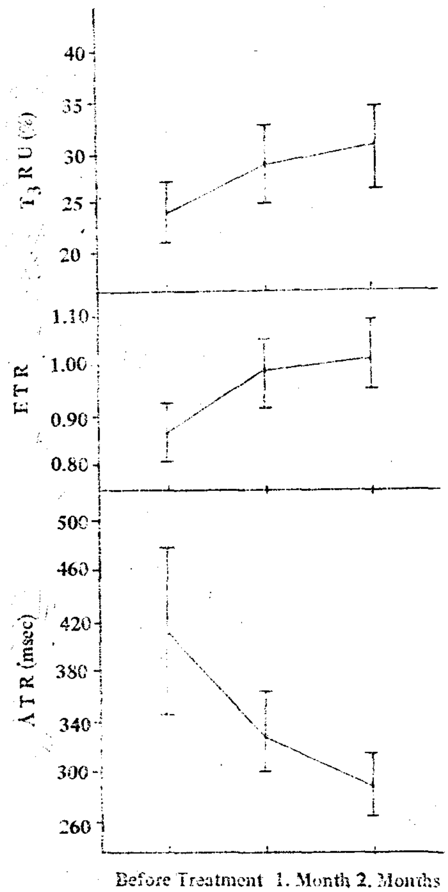

Fig. 11. ATR and TFT in hypothyrodism after treatment with Synthyroid.

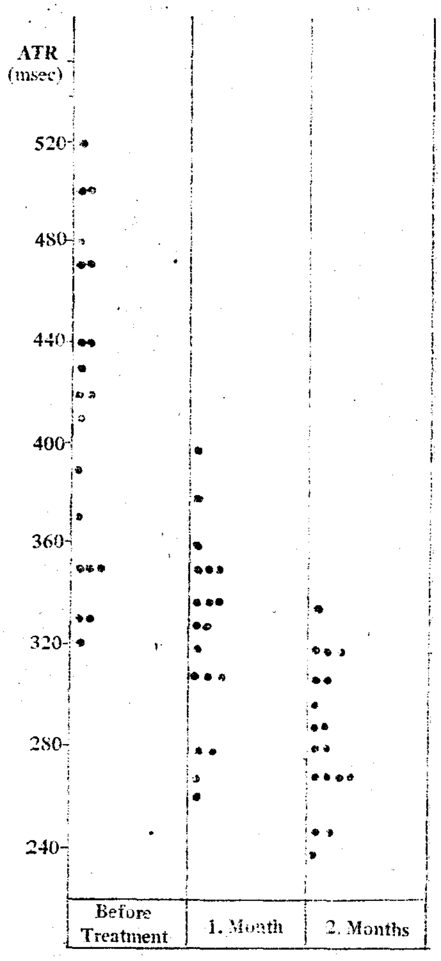

Fig. 12. ATR in hypothyroidism after treatment with Synthyroid.

Discussion

The delayed relaxation of the tendon-jerk in myxedema was first described by Ord[4] (1884) and in 1924 Chaney[1] first measured the tendon reflex time in myxedema. In 1941, Harrel and Daniel, using a pneumatic recording system and the biceps tendon reflex, reported results similar to that of Chaney. However, they measured only the relax phase of the reflex. They found uniform prolongation in five patients with myxedema and also some prolongation in one patient with nephrosis and in one patient with nodular goiter. In addition one man with edema on arm, they found prolongation of the reflex time in a patient with unilateral edema on the arm although the reflex time on the other nonedematous arm was normal.

They concluded that the slowness of relaxation in myxedema was probably due to myxedematous infiltration of the tissues. In 1951, Lambert and associates reported a confirmation and extension of Chaney's original observations in myxedema using an improved, but still somewhat cumbersome recording system. They also examined the muscle action potential and latency period of the Achilles reflex and could demonstrate little change in myxedema from normal. They, therefore, concluded that the slow reflexes seen in myxedema were directly due to changes in muscle function themselves. In 1958, Lawson[5] reported the development of electromagnetic device (Kinemometer) for measuring reflex speed and presented data accumulated in normal individuals and in patients with thyroid diseases. In 1959, Gilson[6] reported on a photoelectric system for reflex recording. Both of those latter instruments are available commercially.

They are simple, convenient, and apparently accurate, and the results can be rapidly obtained. Both measure the free and unhindered Achilles reflex time. Most authors have reported shortening of the duration of the Achilles reflex in hyperthyroidism, but with considerable overlapping with normal individuals. Fogel and associates[7], however, using the photomotograph and the half-relaxation time measurement, reported good separation of hyperthyroid patients from normal individuals.

Since it has been adequately shown that reflex speed varies directly with thyroid function, two major questions arise.

First, what recording device measures these reflex change best? Second, what part or parts of the reflex reflect changes in thyroid function best? Although direct comparisons have not been made, it would appear that any of several devices currently in use adequately measure the mechanical events of the tendon reflex and extend the usefulness of the clinically observed phenomena.

As to the part of the reflex measured, most investigators following the lead of Lambert and associates[2] have used the measurement from the start of the initial stimulus to one half the relaxation time for clinical purposes. This includes all of the contraction phase and half the relaxation phase. Lambert and associates[2] noted the relaxation phase to be affected to the greatest extent in both myxedema and hyperthyroidism. However, the end of the relaxation phase was often hard to determine, so for clinical purposes they measured only to half the relaxation time.

They also noted a characteristic shoulder occurring in the first part of relaxation on their tracings from patients with myxedema that helped produce prolongation of the first half of the relaxation phase and was included in the measurement. But Lawson,[5] using the kinemometer, has emphasized the contraction phase as correlating best with thyroid activity. In our investigations, half the relaxation time was affected to the greatest extent in the myxedema and hyperthyroidism, but in contraction time between thyroid diseases and normal control there were significant differences($P<0.01$).

So we used the measurement which includes all the contraction phase and half the relaxation time for clinical purposes. In myxedema, the mean of Achilles tendon reflex times(414 ± 95msec) was markedly prolonged compared to that of normal control(295 ± 41msec) ($P<0.01$).

And also in thyrotoxicosis the mean (221 ± 20 msec) was significantly shortened compared to that of normal control($P<0.01$).

We examined the changes of ATR times in various thyroid disease patients after treatment and also compared them with their clinical courses and their thyroid function tests. In hyperthyroidism patients who were treated with[131] I and methimazole simultaneously, we observed that their ATR time was in normal range at the second month after treatment. And in cases who were treated with methimazole only, their reflex times were in normal range after 3 months.

We also observed that the changes of ATR times were consistent well with those of clinical courses and thyroid function tests.

In hypothyrodism patients, we treated them with Synthyroid.

Their Achilles reflex times were in normal range in 2 months after treatment and, as in hyperthyroidism, they were consistent well with their clinical courses and thyroid function tests, too.

Therefore, we could conclude that the measurement of Achilles tendon reflex times was very valuable not only in the diagnosis of thyroid diseases but in the evaluation of their clinical courses.

The accuracy of the Achilles reflex test is now under challenge. Lawson and associates[5] have claimed a diagnostic accuracy of 94 to 100% in hypothyroidism and of 63 to 93% in hyperthyroidism.

Lambert and associates[2]. however, reported 77% diagnostic accuracy in hypothyroidism and 25% in hyperthyroidism. This wide variation in diagnostic accuracy may be due to both testing instrument and selection of subjets to be tested. We observed a diagnostic accuracy of 90% in hypothyroidism and 71% in hyperthyroidism.

Furthermore, Achilles reflex test showed no significant overlap between hyperthyroidism and normal control. And also it revealed good correlation with other thyroid function tests, so that we concluded that it is a very valuable adjunct in the diagnosis of thyroid disorders and in following them once treatment is begun.

In normal subjects there is some controversy in the effect of age and sex on the reflex time among many investigators. Some reported the increment of reflex time as age increases[12], but most of others noted no change.[11] There were some reports noting statistically significant mean differences between sexes with female having a longer reflex time. But Fogel and associates noted no effect of sex on the reflex time.[11] We observed significant increment of time as age increases in normal subjects($P<0.01$). And also we noted the tendency of female having a little longer reflex time than male but it was of no significance statistically. There have been some reports concerning the factors which affect the ATR time. These include obesity[2], nephrosis, agitated states, fever, pregnancy, a variety of neurological and neuromuscular disorders, and pernicious anemia.[11] But Fogel and associates[7] reported normal findings in obese persons.

They also noted normal reflex times in pregnancy, fever, agitated states and a variety of neurological and neuromuscular disorders. Lawson[5] reported a variety of disease states in which no significant change in the ATR time was found. But Simpson, Blair and Nartowicz[13] have reported prolonged ATR times in patients with neurosyphilis and in schizophrenia. There are several reports concerning the effects of drugs on ATR time, though there is some controversy in them among several investigators. Lawson[5] reported shortening of the contraction phase of the reflex in normal subjects after the administration of the following drugs; salicylates in high doses, dextroamphetamine sulfate, ACTH, cortisone, thyroid hormones, and estrogens in high doses. Lengthening was noticed with administration of thiourea compounds, perchlorates, and bromides in high doses. Goldberg has reported shortening of contraction phase of Achilles reflex in normal subjects following subcutaneous injection of 0.5mg epinephrine. [11] It would appear that although changes in reflexes as recorded by different authors are not entirely specific for changes in thyroid function, few other disease entities and few drugs cause significant alterations in the phenomenon. We experienced several cases which showed considerable differences between left and right in the measurement of Achilles reflex time. And also we observed several cases which showed no reflex. But we could not find any underlying causes in them. In the present series we realized that measurement of Achilles reflex time is a very valuable adjunct not only in the diagnosis of thyroid disorders but in follow up of these disorders.

Summary

A simplified photoelectric apparatus producing graphic records of the free Achilles tendon reflex allowed us to study the reflex quantitatively in subjects with normal and abnormal thyroid function. In this study Achilles tendon reflex times were tested in 340 normal Korean persons, 89 hyperthyroid patients, 19 hypothyroid patients and 85 other thyroid disease patients who were euthyroid in thyroid function tests. In normal Korean persons, the Achilles tendon reflex time was delayed with increasing age and slower in female than in male. They showed good correlationship with various thyroid function tests which included ETR, T_3RU, ^{131}I thyroid uptake and serum TSH. Diagnostic accuracy of them was 71% in hyperthyroidism and 90% in hypothyroidism.

Finally the serial measurements of them were very useful tests in evaluating the clinical coures of hyperthyroidism and hypothyroidism once treatment was begun.

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=국 문 초 록=

正常韓國人 및 各種甲狀腺疾患에서의 아킬레스腱反射時間에 關한 硏究

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著者는 正常韓國人과 各種甲狀腺疾患에서의 아킬레스腱反射時間을 Photomotograph에 의해 測定하여, 그 診斷的 價値와 韓國人에 있어서의 年齡別, 性別에 따른 正常値를 求하기 위하여 1975年 4月 1日부터 1977年 8月 30日까지 서울大學校 醫科大學 附屬病院 內科를 來訪한 各種 甲狀腺疾患 患者 193例와 正常韓國人 男子 190名, 女子 150名, 총 340名을 對象으로 하여 다음과 같은 結果를 얻었다.

1) 正常韓國人에서의 아킬레스腱反射時間은 11세부터 20세까지는 男子; 250±27 msec, 女子; 266±27 msec, 21세부터 30세까지는 男子; 271±27 msec, 女子; 284±25 msec, 31세부터 40세까지는 男子; 273±25 msec, 女子; 291±27 msec, 41세부터 50세까지는 男子; 286±35 msec, 女子; 307±42 msec, 51세부터 60세까지는 男子; 296±33 msec, 女子; 318±46 msec, 61세 이상에서는 男子; 301±33 msec, 女子; 325±35 msec로서 年齡에 따라 현저히 增加되어 있었으며, 性別에 따른 差는 女子가 남자에 比하여 다소 遲延되는 傾向을 보였으나 有意한 差는 없었다.

2) 甲狀腺機能亢進症 患者에서의 아킬레스腱反射時間은 221±20 msec로서 正常對照群에 比해 현저히 短縮되어 有意한 差가 있었다.

3) 甲狀腺機能低下症 患者에서의 아킬레스腱反射時間은 414±65 msec로서 正常對照群에 比하여 현저히 지연되어 有意한 差가 있었다.

4) 甲狀腺機能檢査上 正常인 甲狀腺疾患 患者에 對한 아킬레스腱反射時間은 287±33 msec로서, 正常對照群에 比하여 有意한 差가 없었다.

5) 아킬레스腱反射時間과 ETR (Effective Thyroxine Ratio), T_3RU, ^{131}I攝取率 및 血中 TSH値와는 밀접한 相關關係를 보였다.

6) 아킬레스腱反射時間의 診斷的 正確度는 機能亢進症에서 71%이었고, 假陽性率은 11%, 假陰性率은 29%이었으며 甲狀腺機能低下症에서의 診斷的 正確度는 90%, 假陽性率은 27%, 假陰性率은 10%이었다.

7) 治療後, 症狀 및 機能의 好轉과 아킬레스腱反射時間사이에는 좋은 相關關係를 보여 甲狀腺疾患의 經過觀察에 有效하였다.