Thyroid Function Studies of Healthy Koreans and Patients with Thyroid Disease by means of I\textsuperscript{131}-Triiodothyronine\textsuperscript{*,**}.

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Since Hamolsky and his coworkers\textsuperscript{1) had} introduced the erythrocyte uptake of I\textsuperscript{131}-labeled triiodothyronine (I\textsuperscript{131}-TRI) as a new thyroid function test, this simple and rapid in vitro test was used and discussed by some other investigators\textsuperscript{2,4,11). On the basis of these clinical data, triiodothyronine in vitro test was known as a method with good diagnostic accuracy in thyroid disease.

The results of the study reported in here primarily concern the use of the red blood cell in vitro incorporation of I\textsuperscript{131}-labeled triiodothyronine from whole blood as an index of thyroid function status in Koreans. The accuracy of this study was compared with other currently used methods such as I\textsuperscript{131} thyroid uptake, PBI\textsuperscript{135} conversion ratio, BMR, serum cholesterol level etc. This report also deals with the summary of thyroid function of normal Koreans from various districts in an effort to find the standard level. Besides, attempts were made to find whether there exist any significant difference in the erythrocyte uptake of I\textsuperscript{131}-TRI according with geographical areas using the in vitro triiodothyronine method.

Materials and Methods

Materials

Blood samples were taken from healthy physicians, medical students, technicians and nurses of Seoul National University and out and in-ward patients of Seoul National University Hospital. Independently

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...thyroid status was determined by clinical evaluation including clinical response to therapy and one or more standard laboratory procedures such as the measurement of BMR, chemical PBI level, 24 hour thyroid-uptake of radiiodine (I\textsuperscript{131}), PBI\textsuperscript{131} conversion ratio and blood cholesterol concentration. Blood samples taken from healthy inhabitants in various districts also were received by male.

Methods

a) Tracer amounts (50×10^{-4}\mu g/0.1ml.) of I\textsuperscript{131}-TRI were added to aliquots in duplicate of the heparinized whole blood in a 15ml. pyrex tube.

b) The tube was then incubated in water bath at 37°C and constantly shaken for 2 hours.

c) With a well-type scintillation counter, the radioactive content of each tube was determined by counting for sufficiently long period as to obtain 2% accuracy.

d) The aliquots were centrifuged, supernatant plasma removed, and red cells were washed 3 times with 5-6 times volumes of isotonic saline.

e) The radioactivity remaining in the r.b.c. fraction was then determined by the method as described in c).

f) The percentile r.b.c. uptake was then calculated as

\text{Erythrocyte uptake in \%} = \frac{\text{net counts in rbc}/3ml}{\text{net counts/3ml of whole blood}} \times 100

The values were corrected to hematocrit reading of 100.

Corrected erythrocyte uptake

\text{erythrocyte uptake} = \frac{\text{erythrocyte uptake}}{\text{hematocrit}} \times 100

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Results

1. Summary of the red blood cell uptake of $^{131}$I-triiodothyronine from whole blood of normal Koreans and geographical relations

Table 1. The 2 hr. in Vitro r.b.c. uptake of $^{131}$I-TRI from whole Blood of Healthy Koreans

<table>
<thead>
<tr>
<th></th>
<th>Men</th>
<th></th>
<th>Women</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>r.b.c.</td>
<td>No. of case</td>
<td>r.b.c.</td>
<td>No. of case</td>
</tr>
<tr>
<td>Average</td>
<td>9.7—24.8</td>
<td>154</td>
<td>8.5—21.8</td>
<td>143</td>
</tr>
<tr>
<td>S. D.</td>
<td>3.24*1</td>
<td>3.56*2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less than Normal Range</td>
<td>10%</td>
<td>1 (0.64%)</td>
<td>10%</td>
<td>3 (2.10%)</td>
</tr>
<tr>
<td>Less than 11%</td>
<td>44 (28.57%)</td>
<td>44 (28.57%)</td>
<td>18 (12.59%)</td>
<td></td>
</tr>
<tr>
<td>Normal Range</td>
<td>&gt;19%</td>
<td>7 (4.54%)</td>
<td>&gt;19%</td>
<td>4 (2.80%)</td>
</tr>
</tbody>
</table>

Fig. 1. Distribution of the r.b.c. uptake of $^{131}$I-TRI in vitro from whole blood of normal Koreans

The results of thyroid function test in 154 euthyroid males and 143 females were shown in Table 1. The in vitro red blood cell uptake of $^{131}$I-triiodothyronine in males ranged from 9.7% to 24.8% averaging 15.7±3.24 percent. In females, the uptake ranged from 8.5% to 21.8%, averaging 14.4±56 percent. The data indicates that the erythrocyte uptake in males was significantly higher than in females.

Table 2. Age Distribution of r.b.c. Uptake in Normal Koreans

<table>
<thead>
<tr>
<th>Age</th>
<th>Average (%)</th>
<th>S.D.</th>
<th>Average (%)</th>
<th>S.D.</th>
</tr>
</thead>
<tbody>
<tr>
<td>10—19</td>
<td>15.30</td>
<td>2.49</td>
<td>13.98</td>
<td>1.66</td>
</tr>
<tr>
<td>20—29</td>
<td>15.90</td>
<td>3.26</td>
<td>14.60</td>
<td>2.27</td>
</tr>
<tr>
<td>30—39</td>
<td>16.90</td>
<td>4.14</td>
<td>14.50</td>
<td>4.72</td>
</tr>
<tr>
<td>40—49</td>
<td>15.30</td>
<td>1.82</td>
<td>12.70</td>
<td>2.09</td>
</tr>
<tr>
<td>50—59</td>
<td>14.50</td>
<td>2.19</td>
<td>11.60</td>
<td>1.25</td>
</tr>
<tr>
<td>60—69</td>
<td>11.80</td>
<td>1.40</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Fig. 2. Age Distribution of r.b.c. uptake in Normal Koreans

The effect of age upon thyroid function was shown in Table 2 and Fig. 2. In both sexes, the uptake was low in the older individuals. The decline of erythrocyte uptake in euthyroid females just before menopause was significant.

Data from various areas are summarized in Table 3. Except two areas of islands, Jeseu and Jindo, blood samples were taken from inhabitants in urban areas. No significant differences in r.b.c. uptake according with geographical areas were found either in males or females. In Jindo, blood samples were
Fig. 3. Comparative values of r.b.c. uptake of I\textsuperscript{131} TRI with Various Districts of Korea

Table 3. Summary of comparative values of I\textsuperscript{131} TRI, r.b.c. uptake with various districts of Korea.

2. The effect of pregnancy

Of 26 pregnant females, the r.b.c. uptake of triiodothyronine was consistently decreased throughout the entire period of pregnancy, as shown in Table 4. and Fig. 4.

The r.b.c. uptake averaged 9.1±1.71 percent, ranging from 7.8 to 15.0 percent. In one woman, measurements of r.b.c. uptake were performed before and during pregnancy, and in another woman during and after pregnancy. In the former, the value was decreased from 12.6 percent before pregnancy to 9.3 and 9.7 percent after the first and 3rd month of gestation respectively. In the latter, r.b.c. uptake during pregnancy(8.6%) was restored to 13.6 percent two weeks after delivery. Besides, one patient with eclampsia showed 15.0 percent of r.b.c. uptake at the 6th month of pregnancy.
thyroid uptake of 24 hours, PRI\textsuperscript{131} conversion ratio of 24 hours, BMR and serum cholesterol were 54.1 percent, 58.0 percent, 37.4 percent and 109.6mg percent respectively.

The value that fell within normal range was one in PBI\textsuperscript{131}-TRI test, one in PBI\textsuperscript{131}-thyroidal uptake of 24 hours, one in PBI\textsuperscript{131} conversion, one in BMR and none in cholesterol level.

Average value of r.b.c. \textsuperscript{131}TRI uptake of 36 cases of female hyperthyroidism was 23.5 percent, and average values of \textsuperscript{131}TRI-thyroidal uptake, PBI\textsuperscript{131} conversion ratio, BMR, cholesterol level were 65.3 percent, 62.6 percent, 28.0 percent and 123.8mg percent respectively. The values that fell within normal ranges were one in \textsuperscript{131}TRI test, in \textsuperscript{131}TSH uptake test.

3. Comparative study of r.b.c. uptake test with other currently used methods in toxic and nontoxic goiter

The results are summarized in tables 5 and 6. In seven hyperthyroid males, average value of r.b.c. \textsuperscript{131}TRI uptake was 27.6 percent, mean values of \textsuperscript{131}TRI-thyroidal uptake, in 3 PBI\textsuperscript{131} conversion ratio, 7 in BMR and 4 in cholesterol level.

Average value of r.b.c. \textsuperscript{131}TRI uptake was 14.2 ± 2.47 percent in 12 cases of male nontoxic goiter 14.2±3.12 percent in 43 female cases.

These data have been compared favorably with
Table 6. The r.b.c. Uptake of $^{131}I$ TRI Compared with other Thyroid Function Tests in Non-Toxic Patients.

<table>
<thead>
<tr>
<th>sex</th>
<th>Subjects</th>
<th>T.F.T.</th>
<th>r.b.c. uptake of $^{131}$TRI</th>
<th>$^{131}$-Thyroid uptake (24hrs.)</th>
<th>P.B.I. C-R (24hrs.)</th>
<th>B.M.R.</th>
<th>Cholesterol (total)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>No. of cases</td>
<td>12</td>
<td>12</td>
<td>12</td>
<td>11</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td></td>
<td>range</td>
<td>10.2~17.9</td>
<td>6.3~64.3</td>
<td>3.2~69.4</td>
<td>-5~+36.5</td>
<td>90.3~200(mg)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>mean Value</td>
<td>14.2</td>
<td>23.9</td>
<td>22.7</td>
<td>+13.2</td>
<td>160.1(mg)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>S.D.</td>
<td>2.47</td>
<td>18.2</td>
<td>19.5</td>
<td>12.7</td>
<td>47.2(mg)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>No. of cases</td>
<td>&lt;11% &lt;10%</td>
<td>&lt;10%</td>
<td>&lt;10%</td>
<td>&lt;-15%</td>
<td>&lt;140(mg%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>showed above or less &lt;18.3% 2(16.7%)</td>
<td>2(16.7%)</td>
<td>1(8.3%)</td>
<td>0(0%)</td>
<td>1(10%)</td>
<td>1(50%)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>No. of cases</td>
<td>43</td>
<td>43</td>
<td>43</td>
<td>35</td>
<td>35</td>
<td></td>
</tr>
<tr>
<td></td>
<td>range</td>
<td>8.5~17.6</td>
<td>4.7~60.2</td>
<td>2.7~68.5</td>
<td>-19~+52</td>
<td>91.4~232(mg)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>mean Value</td>
<td>14.2</td>
<td>26.1</td>
<td>25.6</td>
<td>13.5</td>
<td>169.6(mg)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>S.D.</td>
<td>3.12</td>
<td>15.8</td>
<td>17.0</td>
<td>19.2</td>
<td>53.9(mg)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>No. of cases</td>
<td>&lt;11% 5(11.6%)</td>
<td>&lt;10% 6(14.0%)</td>
<td>&lt;10% 5(11.6%)</td>
<td>&lt;-15% 3(8.6%)</td>
<td>&lt;140(mg%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>showed above or less &gt;17% 2(4.7%)</td>
<td>&gt;40% 6(14.0%)</td>
<td>&gt;45% 6(14.0%)</td>
<td>&gt;15% 15(42.9%)</td>
<td>&gt;240(mg%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Fig. 5. Relation between r.b.c. Uptake of $^{131}$-TRI and $^{131}$-thyroid Uptake

those of currently used methods. As shown in Table 6, the values surpassing the normal range in r.b.c. TRI test was one from 12 male patients(8.35%) and was 7 from 43 female patients(16.3%).

The distribution of TRI test in female subjects with toxic and nontoxic goiter is shown in Fig. 6. Although 2 women (4.7%) with nontoxic goiter showed higher values than normal range, and 5 women (11.6%) showed lower values than normal, most values of TRI test in nontoxic goiter were within normal range. And values in toxic goiter group were significantly high when compared with euthyroid group and nontoxic goiter group. Correlations between the values of TRI test and those of other function test are not apparent except minor
correlation between values of TRI test and $^{131}$
thyroid uptake as might be seen in Fig. 5.

4. Hypothyroidism and the effect of thyroid 
administration to hypothyroid subjects

Table 7. The results of thyroid function test 
compared with various laboratory data in 14 
hypothyroid patients.

<table>
<thead>
<tr>
<th>Pts.</th>
<th>Treatment</th>
<th>T.F.T. RBC uptake</th>
<th>$^{131}$-TRI uptake</th>
<th>P.B.I C-r</th>
<th>B.M.R. %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pt. A</td>
<td>before</td>
<td>5.4</td>
<td>4</td>
<td>6.1</td>
<td>-5</td>
</tr>
<tr>
<td>F: 40</td>
<td>after 1.5M</td>
<td>14.9</td>
<td>6</td>
<td>3.8</td>
<td>+10</td>
</tr>
<tr>
<td>Pt. B*</td>
<td>before</td>
<td>10.3</td>
<td>0.1</td>
<td>7.7</td>
<td>3</td>
</tr>
<tr>
<td>F: 40</td>
<td>after 1M</td>
<td>22.7</td>
<td>4.4</td>
<td>10.1</td>
<td>25</td>
</tr>
<tr>
<td>Pt. C</td>
<td>before</td>
<td>6.8</td>
<td>2.6</td>
<td>5.3</td>
<td>-30</td>
</tr>
<tr>
<td>F: 55</td>
<td>after 2M</td>
<td>16.9</td>
<td>9.5</td>
<td>20.0</td>
<td>-11</td>
</tr>
<tr>
<td>Pt. D</td>
<td></td>
<td>6.4</td>
<td>15</td>
<td>11.2</td>
<td>-6</td>
</tr>
<tr>
<td>M: 53</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Sinus tachycardia (Premature beat).

Of 4 hypothyroid cases, red cell uptake of TRI was 
significantly lower than in euthyroid subjects except 
that one patient showed 10.3 per cent approaching 
the lower border of normal spectrum (Table 7). $^{131}$ 
thyroid uptake of 24 hours, PBI$^{33}$ conversion ratio 
and BMR were also significantly decreased in hypothyroidism, but no correlation on the value of r.b.c. 
TRI uptake was found.

In tests of r.b.c. TRI uptake during the administration 
of desiccated thyroid tablets, a significant increase in $^{131}$TRI erythrocyte uptake were found in 
all cases.

From the results described above, it may be said 
that $^{131}$ thyroid uptake, PBI$^{33}$ conversion ratio and 
BMR were less reliable as diagnostic tests when compared with RBC-TRI test.

Discussion

As indicated by Robbins$^{32}$, laboratory tests of 
thyroid function have been increasing importance, 
for the routine examinations in the population at large. There are many parameters of thyroid function 
currently in use, but the test of the red cell 
uptake of $^{131}$-TRI is simple and rapid in its procedure 
and is convenient as a screening procedure.

However, it is necessary to evaluate the diagnostic 
accuracy of this test in comparison with that of 
other methods. The results of comparative studies 
were summarized by Bauer$^{30}$ and discussed by 
Hamolsky$^{1,4}$ and Robbins$^{32}$. Numerous papers that 
followed the study dealt with possible mechanism of 
RBC-TRI and its variance with thyroid status$^{5-10}$.

From the results as illustrated in Table 1 to 6, it is apparent that the spectrum of normal range 
was rather narrow when compared with that 
obtained by other currently used methods and overlapping of the ranges among euthyroidism, hypothyroidism and hyper-thyroidism were less frequently 
encountered than that of other laboratory data$^{11}$.

In attempts to find whether there exists geograph- 
ical difference in thyroid function in several area 
of Korea, no difference among various districts was found. The distribution of thyroid patients that 
visited the Clinic of Seoul National University Hospital was observed by Kim et al$^{12}$ and they 
concluded that there was no significant variance 
according with different areas.

The levels of normal range and decrease in r.b.c. 
uptake in females as observed in this study well 
corresponded with the results obtained by other workers. Slightly higher values in this study when 
compared with data from Hamolsky et al$^{10}$, might have been resulted from thrice washing instead of 
their four time washings of erythrocytes and other minor differences in experimental procedures.

Effects of pregnancy on the erythrocyte uptake 
of TRI was observed by Hamolsky$^{1-4}$ and Robbins$^{32}$.
The decrease of erythrocyte uptake during pregnancy 
has been explained on the basis of an increase 
in specific binding globulin of plasma$^{33-36}$. In our 
experiment, the reversal of erythrocyte uptake after delivery and the influence of eclampsia during 
pregnancy were observed. Other factors that may 
be concerned with these changes may include alterations of plasma protein pattern, carbon dioxide 
retension and estrogen level in blood.

The erythrocyte uptake of $^{131}$-TRI may prove to be a fairly accurate indicator in the course of follow 
up studies in hypothyroidism treatment. The effect 
of thyroxine and triiodothyronine concentrations in the plasma on the uptake of these hormones into 
erythrocyte and the tissue cells were studied in experimental animals as clinically by several 
workers$^{1-6}$.

In this study, clinical improvement following the
administration of thyroid tissue went parallel with the increased uptake of erythrocyte. With other methods currently in use, however, the tests did not always reveal the favorable results of therapeutic administration of thyroid extract. On the basis of these findings, it may be concluded that the uptake of TRI into erythrocyte best reflects therapeutic effect of thyroid hormone administered against hypothyroidism.

**Summary**

The in vitro erythrocyte uptake of I\(^{131}\)-TRI was determined in normal Korean subjects and patients with thyroid diseases. Concomitantly, other laboratory tests currently in use were performed in patients.

1. Erythrocyte uptake of I\(^{131}\)-TRI averaged 15.7±3.24 percent in normal males and 14.4±3.56 percent in normal females. No significant difference in erythrocyte I\(^{131}\)-TRI values according with various geographical areas of Korea was found.

2. Erythrocyte uptake of I\(^{131}\)-TRI was decreased during pregnancy and restored after delivery.

3. Accuracy of erythrocyte I\(^{131}\)-TRI uptake test as a diagnostic aid was compared with that of other currently used methods in patients with toxic and nontoxic goiter.

4. The value of erythrocyte I\(^{131}\)-TRI were significantly decreased in hypothyroid patients and administration of thyroid extract resulted with the increase in the value.

**REFERENCE**


8) Dinglelina, W.S., P-Rivers, R. and Stanburg, J.B.


