First Report on External Quality Assurance Study of Radioassay of Thyroid Related Hormones

— First One Year of Operation From 1989. 9 To 1990. 8 —

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== 국문초록 ==

갑상선 호르몬의 외부정도 관리 분석

—1989년 9월부터 1990년 8월까지 첫해 시행 결과—

서울대학교병원 핵의학과

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1989년 9월부터 1990년 8월까지 국제 원자력기구의 지역 계획에 의해 국내 26개(후반부 31개)의 기관이 참가하여 T3, T4, TSH를 측정하여 결과를 모으고, 외부정도관리를 시행한 결과가 다음과 같다.

1) 외부정도관리를 위한 컴퓨터 소프트웨어를 작성하였다. 데이타의 입력, 정도 분석, 월별 보고, 분기별 보고 및 수행 분석 프로그램을 만들되 전체 검사실결과에서 추린 평균값(all laboratories trimmed mean: ALTM)으로 모집단평균을 삼아 편차, 편이, 편이평균 그리고 이들의 경시적 변화를 분석하도록 하였다.

2) 전후반 2회에 나누어 만든 뱃치 사이의 편차는 유의하지 않았다. T3 값의 변이계수는 7.2%이하(정상 T3 값) 또는 9.2%와 13.4%사이(높은 T3 값), T4 값의 변이계수는 4.6%이하(정상 또는 높은 T4 값), 5.4%와 9.5%사이(낮은 T4 값)이었다. TSH는 정상범위 값에서 21.7%이하의 변이계수를 보였고 정상보다 낮거나 높은 TSH의 풀은 8.7%와 21.2%사이의 변이계수를 보였다.

3) 전체 검사실 추린 평균값(ALTM)에 따른 변이계수의 변동은, ALTM이 정상 T4 값범위일 때 변이계수는 15%이하이었고, 낮은 T4 값일 때는 중간값이 15%이고 분포범위는 50%까지이었다. T3 값의 변이계수는 대체로 20%이하이었다. TSH의 변이계수는 1 mU/L를 전후로 급격히 상승하여 200%에 달하였다.

4) 3표준편차보다 높거나 낮은 값을 보인 검사실들의 분포는 전체 검사실결과에서 추린 평균값(ALTM)과 상관없었다.

5) 첨가한 T3, T4, TSH에 대한 회수율은 T4는 104, 106%, T3는 67%, 74%, TSH는 87%, 86%이었다.

이상과 같이, 저자들이 만든 소프트웨어 프로그램으로 외부정도관리를 위하여 쉽게 데이터를 분석 하고 보고서를 작성하여 갑상선호르몬의 검사신뢰도를 평가할 수 있게 되었으며, 위에 요약한 첫 해 의 외부정도관리 결과를 바탕으로 참가기관의 동의하에, 앞으로 정도관리 항목의 확대와 외부정도관 리의 지속적인 시행이 바람직하다고 생각하였다.

INTRODUCTION

Internal quality control of radioassay has been emphasized since the advent of radioimmunoassay since 1960's. It is not only because the nuclear laboratory physicians need to be convinced with the results they have produced, but because the referring clinicians should be assured with the reports of hormone assays they got from nuclear laboratories every day.

For the internal quality control, we usually add to our every assay at least three batches, and it is recommended that we should disregard our total assay results if one of the batch results is over 3 standard deviation (SD), if two of the batch results are over 2 SD, or if all the three are over 1 SD. But even when this surveillance system is working on, questions still remain whether our results were not discrepant from those of the other laboratories or not. In other words, the nuclear physicians or the referring clinicians used to wonder if they could count on the assay results that they have received from the neighboring physicians[1].

There are two ways to control the quality of the assays in these aspects. One is solely up to individual laboratories' efforts, that is, one could buy sera or plasma sold as commercialized controls whose concentrations are known. The other is running external quality control, nationally or regionally[3~10]. International Atomic Energy Agency (IAEA)[11] started external quality control in Asian countries since September of 1989. And it included three regional centers and 11 countries. Our Nation participated in the project (RAS 6/011) as regional center covering the laboratories of our Country and those of Philippines and Malaysia.

Three hormones were measured by 26 (first half of operation) or 31 (second half) laboratories from our Nation and 5 labs from Malaysia and 8 from Philippines. After the completion of despatching samples and gathering results, one of authors (Kwark C) has worked out algorhithm on personal computer by Turbo BASIC[12,13] with Graphics to manage the data for external quality control study (EQAS). We are now running the second year of operation and are expecting the third year operation starting from April of 1992 according to the planning of IAEA. This is the report of the first year operation of our country and our region and the explanation of the interpretations of the reports of software. The reports of the second and the third years will follow soon after the completion of each operation.

METHODS

1. Description of Laboratories and Methods

1) Characteristics of the Participants

26 laboratories participated in the first half of the first year operation of IAEA EQAS from our Nation. For the second half of the first year operation, the enlisted laboratories increased to 31, but only 28 among 31 (90.3%) reported the results. For the second half of the first year operation, 1 out of the 26 laboratories had been dropped out. But after they received the reports from the center, this laboratory rejoined the project for second year operation (Table 1, 2).

Among 26 Korean laboratories who started the

Table 1. Number of Laboratories

	Labs enlisted	Labs reported	reported/ enlisted
1st 6month	26	26	100%
2nd 6month	31	28	90.3%

Table 2. Participating Laboratories from our Nation
A. Types of Laboratory

	1st 6 month	2nd 6 month
University Hospital	11 (42.3%)	14 (45.2%)
General Hospital	11 (42.3%)	13 (41.9%)
Private Clinic	4 (15.4%)	4 (12.9%)
	26 (100%)	31 (100%)

B. Types of Service

Nuclear Medicine	13 (50.0%)
Clinical Laboratory	9 (34.6%)
Endocrine Laboratory	4 (15.4%)
	26 (100%)

EQAS, 84.6% were those of university or general hospital and the rest (15.4%) were the laboratories of private clinics. Thyroid function tests were performed mostly, 50%, in the Departments of Nuclear Medicine, 34.6% in the Departments of Clinical Laboratory Medicine. The 15.4% of these laboratories were the specialized research laboratories for clinical endocrinology. Table 3 is the list of participating laboratories.

2) Assay Methods

Table 4 describes the methods of thyroid function tests used by the participating laboratories at the start. All the laboratories used commercialized kits except one. Abbott kits were used most widely for radioimmunosassay of T3 or T4. All the laboratories except one measured TSH by IRMA method with commercialized kits. Dainabott products for TSH were the most widely used (Table 4).

Table 3. List of Participating Laboratories

College of medicine, Kyung-hee university,
Korea general hospital,
Kwangju Christian hospital,
Green cross clinical pathology,
Taegu Fatima hospital,
Buchun Seongga hospital,
Samkwang reference laboratories,
Seoul National University Hospital,
Seoul clinical laboratories,
Dong boo city hospital,
Seoul jungang hospital,
College of medicine, Yonsei university,
College of medicine, Yeungnam univeristy,
Wonkwang university hospital,
Korea cancer center hospital,
Ewon yanghaeng corporation,
Inje medical college, Busan paik hospital,
Seoul paik hospital, Inje medical college,
Incheon Christian hospital,
In ha hospital,
Jeonnam national university, Medical school,
Cheil general hospital,
Kangnam general hospital public corporation,
Baptist hospital,
Korea veterans' hospital,
College of medicine, Hanyang university,
Soonchunhynag medical college,
Jeonbuk national university, Medical school,
Hamchun clinical pathology,
Hae jeong hospital,

2. Calculations of Parameters[13,14]

For calculation of all laboratories trimmed mean (ALTM), standard deviation (SD), coefficient of variation (CV), mean bias, and variability of bias, the lowest and highest 5% of results of all the laboratories were trimmed off. So, the excluded values played no part in the calculations of mean value and dispersion of values. Bias of each assay was calculated; the value of each lab was subtracted by the ALTM and then this value was divided by ALTM. The distribution of bias was presented by the mean and variability of each assay.

Table 4. Methods Used by Laboratories at the Start

	T3	T4	TSH
	kit No	kit No	kit No
Commercialized kits	25 (13 Abbott)	25 (13 Abbott)	26 (14 Dainabot)
In-house prepared kits	1	1	

Table 5. The Preparation and Distribution of Pools for Each Month

A. Distribution   B. Preparation

	Sample	1	2	3	4	5	Pools	
September,	1989	1A,	2	3	1A	5	1A	Normal euthyroid (Bangkok)
October,	1989	6	7A	8A	1A	2	1B	Normal euthyroid (Lahore)
November,	1989	1B	4	5	1B	3	2	$1A + 50 \ nm/L \ T_4$
December,	1989	6	7A	8A	1A	1B	3	$1A + 100 \ nm/L \ T_4$
January,	1990	1B	4	5	7B	8B	4	$1B + 1.5 \ nm/L \ T_3$
February,	1990	1A	2	3	x	8A	5	$1B + 3.5 \ nm/L \ T_3$
March,	1990*	5	1A	3	7B	1B	6	T_3 suppressed
April,	1990*	1B	2	7B	3	2	7A	T_3 suppressed + 15 mU/L TSH
May,	1990*	4	3	1A	2	5	7B	TRH stimulated
June,	1990*	1B	6	8B	6	1A	8A	T_3 suppressed + 5 mU/L TSH
July	1990*	6	1B	8B	7A	4	8B	TRH stimulated + T_3 suppressed (50:50)
August,	1990*	1A	8A	6	8A	1B		

* Pools were made twice, so the same batch samples were used only among the pools of the first 6 months and among those of the following 6 months.

For the calculation of individual bias, those values omitted for the calculation of ALTM's or etc., were retrieved and were included in the report.

RESULTS AND DISCUSSION

1. Performance of Laboratories

1) Report of Data for Individual Laboratories

We, the three regional centers, located at Seoul, Pakistan and Thailand, distributed all the samples in blind modes (Table 5A). Participating laboratories did not know anything about the preparation and the matrices of each sample (Table 5B).

One of the reports for one laboratory was demonstrated in Fig. 1., the first page of the original report form and the last page. Following the lab code and the name of the laboratory, the name of the pool was

disclosed, to which each sample belonged. The results obtained by each laboratory was listed on the upper row. The ALTM, SD, bias mean (%) and SD and CV of biases followed. The bias of each laboratory was listed below.

Check list for each laboratory followed the report. There was displayed which was the outliers over 3 SD of ALTM for each hormone. The outliers over 3 SD were listed.

2) Performance of Laboratories[15]

Each month, for each hormone asay, the summary of the performances of individual laboratories were listed. These summary sheets were used as a reference for the overview (Fig. 2A). Summary of ALTM, SD, CV of both assay values and their biases were added at the lower rows. At the end of this form, the summary of the number of participating labs, and

Table 6. Reproducibility of All Laboratories Trimmed Mean (ALTM) for the Whole Year

Pool	No. of distribution	T3		T4		TSH	
		ALTM nM	C.V. %*	ALTM nM	C.V. %*	ALTM mU/L	C.V. %*
1A	9	1.85	3.7	94.4	2.3	1.40	5.7
2	6	2.87	2.8	147.8	1.2	1.51	3.8
3	6	2.42	3.6	198.7	1.6	1.51	2.9
1B	9	1.92	25.3	68.9	5.4	1.93	79.0
4	4	2.95	7.2	71.9	5.8	1.13	10.4
5	4	4.55	12.6	71.5	9.5	1.36	21.7
6	8	4.07	9.2	75.5	4.4	0.25	21.2
7A	3	3.65	13.4	71.5	3.8	13.38	10.3
7B	3	1.73	3.4	104.1	1.4	25.91	8.7
8A	6	3.81	9.9	71.2	3.4	4.57	10.4
8B	2	2.55	4.7	87.3	4.6	10.82	21.2
Mean (C.V.)			8.7		3.9		17.7

* The CV for each sample contained the between assay variation. It also had the between-batch variation as well as within-batch variation because each pool consisted of two batches which had been used for two 6 - month - duration operations.

ALTM, SD and CV followed (Fig. 2B).

Performance of participating laboratories were drawn in three different ways. At first (Fig. 3A), the values reported by individual laboratories were displayed in groups, i.e., five samples for T3, T4 and TSH repectively. The second was the drawing of histogram type (Fig. 3B). The frequency of values were drawn with the mean and lines of 3 SD. In this figure one could count the outliers below or above 3 SD of ALTM. Figure 3C figured out the biases of every laboratory. In the figures 3A and 3C the laboratories had their own points at abscissa[16].

2. Reproducibility Within Batch and Between Batch

The ALTM for each pool assayed on more than one occasion was summarized in Table 6. Table 6 is table version of summary similar to the following figures of section 3. We had prepared batches of pools two times for the first year operation. Because of the drift of the ALTM's between batches, the CV's of ALTM's for all the pools had increased slightly, comparing these results (12 months' results) with the ones of the first half of the operation (Table 7).

As far as between-or-within-batch trends are concerned, for T3, pools of 4, 5, 6, 7A, and 8A showed mild drift toward the more concentration in each pool in the second batches. For T4, pools of 4, 5 showed mild upward drift, too. TSH showed also upward drift with pools of 7A, 8A and 8B. The between and within batch drift of TSH was somewhat unique in that the concentration increased more and more by the end of the first year operation in pool 1B.

For T3, the CV's of pools, the concentrations of which were within normal range (1.53 to 3. 38 nM; 100 to 220 ng/ml) (1A, 1B, 2, 3, 4, 7B, 8B) were less than 7.2% variation except pool 1B (11.6%: this value was obtained after sample 5 of August of 1989 were excluded, because only 5 laboratories responded for this pool 1B of August, 1989, sample 5). For the pools (5, 6, 7A, 8A) with high T3 concentration, the CV's ranged from 9.2% to 13.4%.

For high T4 pool (1B), CV was 2%. Normal T4 pool (84.7 to 177.2 nM; 6.6 to 13.8 µg/ml) (1A, 2, 7B, 8B) had CV's less than 4.6%. All the assays for T4

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*******************************************************************
*            IAEA EQAS FOR THYROID-RELATED HORMONES        *
*             ---   IAEA project  RAS/6/011  ---            *
*    ++++++++++++++++++++++++++++++++++++++++++++++++++++   *
*    ...............IMMUNOASSAY LABORATORY..............    *
*    ..........DEPARTMENT OF NUCLEAR MEDICINE..........     *
*    ........SEOUL NATIONAL UNIVERSITY HOSPITAL........     *
*    ............SEOUL, THE REPUBLIC OF KOREA...........    *
*******************************************************************
         LAB. CODE : K18     LAB. NAME : xXy\qRwWm^nXw^
```

POOL	DISTRIBUTION	Sm.No.	T3(nM/l)	T4(nM/l)	TSH(uU/ml)
1	Jan.,1991	S-1	2.00	93.95	1.80
		A.L.T.M.	2.05	84.37	1.68
		S.D.	0.27	8.88	0.50
		C.V.	0.13	0.10	0.29
		BIAS MEAN(%)	+2.88	+1.69	-9.66
		S.D.BIAS	13.52	13.57	22.94
		C.V.BIAS	+4.69	+8.03	-2.37
		YOUR BIAS(%)	-2.47	+11.35	+6.99
3		S-2	2.15	159.59	1.90
		A.L.T.M.	2.10	139.43	1.62
		S.D.	0.21	13.66	0.44
		C.V.	0.10	0.10	0.27
		BIAS MEAN(%)	+2.54	+2.15	-9.43
		S.D.BIAS	15.08	14.85	17.27
		C.V.BIAS	+5.93	+6.91	-1.83
		YOUR BIAS(%)	+2.43	+14.45	+17.38
4		S-3	2.30	195.62	2.00
		A.L.T.M.	2.34	181.24	1.60
		S.D.	0.26	17.34	0.39
		C.V.	0.11	0.10	0.25
		BIAS MEAN(%)	+4.05	+0.36	-5.22
		S.D.BIAS	15.18	12.55	21.54
		C.V.BIAS	+3.75	+35.23	-4.12
		YOUR BIAS(%)	-1.33	+7.94	+25.25
5		S-4	3.23	83.65	1.50
		A.L.T.M.	2.90	84.98	1.61
		S.D.	0.37	9.82	0.44
		C.V.	0.13	0.12	0.27
		BIAS MEAN(%)	+3.00	+0.55	-6.83
		S.D.BIAS	14.63	14.25	24.05
		C.V.BIAS	+4.88	+25.76	-3.52
		YOUR BIAS(%)	+11.26	-1.53	-6.69
6		S-5	4.99	86.23	1.50

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*******************************************************************
**************** CHECK LIST FOR YOUR LAB.[K18] REPORT ************
*******************************************************************
YOUR LAB. HAS BEEN 3 S.D. OUTLIER FOR [ T4   SAMPLE # 1 ] IN Jul., 1991
-----------------------------------------------------------------
                                [ T4   SAMPLE # 5 ] IN Jul., 1991
-----------------------------------------------------------------
              THANK YOU VERY MUCH FOR CONTRIBUTION
                            FROM
    +++++++++++++++++++++++++++++++++++++++++++++++++++++++++
    +++++++++ THE REGIONAL CENTER OF IAEA EQAS PROJECT +++++++++
    +++++++++++++++++++++++++++++++++++++++++++++++++++++++++
    ++++ .............IMMUNOASSAY LABORATORY.............. ++++
    ++++ .........DEPARTMENT OF NUCLEAR MEDICINE.......... ++++
    ++++ ........SEOUL NATIONAL UNIVERSITY HOSPITAL........ ++++
    ++++ ............SEOUL, THE REPUBLIC OF KOREA........... ++++
    +++++++++++++++++++++++++++++++++++++++++++++++++++++++++
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Fig. 1. Report of data for each laboratory. This figure shows only the first page and the last page of the data of labororatory result.

B

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***** IAEA EQAS Report for Jan., 1991 *****
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Fig. 2. Performance of participating laboratories. Each lab is labelled with one code. A) Summary of the performance of the participating laboratories of each month is listed. ALTM, SD, CV and mean bias (%) and variability of bias were listed at the lowest row. B) Summary of each sample for T3, T4 and TSH. This page included outliers, maximum and minimum values.

gave the CV's less than 10%.

For the pools with normal TSH (0.4 to 4.0 mU/L), ALTM's of which ranged from 1.13 to 1.51 mU/L, the CV's ranged from 3% to 44.4% (44.4% instead of 79. 0% in the table: this value was obtained after sample 5 of August of 1989 were excluded because only 5 laboratories responded for the pool 1B of August,

1989, sample 5). Though we took the variation between batch into consideration, this fluctuation was thought to be too much. The reason why some of the pools had so large CV's should be disclosed. For TSH of the pools with increased (pools 7A, 8A, 7B and 8B) or decreased (pool 6) values, the CV's were 8.7 to 21.2% and 21.2% respectively. Pool 8B had
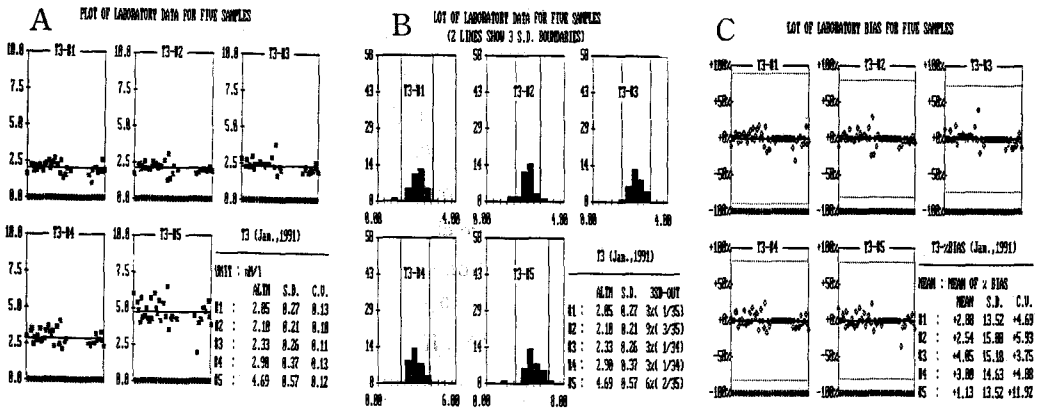

Fig. 3. A) Plot of laboratory data for T3, T4 and TSH of each month. Data about T3 was shown. Abscissa denoted participating 39 laboratories. B) Histogram of results for T3 of the five samples of each month. Abscissa is concentration. Ordinate means the frequency of samples with that concentraion. Two lines show 3SD of ALTM. C) Biases of every laboratory. Dotted lines show 3 SD of mean of biases of all laboratories.

Table 7. Reproducibility of All Laboratories Trimmed Mean (ALTM) for the First Half

Pool	No. of distribution	T3		T4		TSH	
		ALTM* nM	C.V.# %	ALTM* nM	C.V.# %	ALTM* mU/L	C.V.# %
1A	5	1.91	2.9	93.9	1.4	1.32	6.7
2	3	2.09	4.3	149.1	2.4	1.53	4.2
3	3	2.48	2.3	200.4	2.9	1.48	4.4
1B	4	1.85	2.3	69.1	7.2	0.94	15.5
4	2	2.75	0.8	67.9	2.9	0.98	19.6
5	2	4.04	0.9	63.6	3.6	1.01	19.0
6	4	3.77	7.4	78.2	7.7	7.22	47.0
7A	2	3.33	4.9	69.9	4.8	12.61	4.4
8A	3	3.50	6.9	71.2	6.5	4.06	3.8
Mean (C.V.)			3.2		4.0		9.7

* : mean ALTM for each pool distributed more than once.
\# : variability of ALTM for each pool distributed more than once.
Mean CV : mean variability of all ALTM
** : pool 6 was excluded for the calculation of mean CV

been assayed only twice once in the first half and once in the second half of the year. So the CV of this pool was not taken into consideration.

For every pool, the trends of ALTM and SD had been drawn. In Fig. 4A, one could read the 12-month-trend of each pool. Because we had prepared the batch of each pool twice for the first year operation,
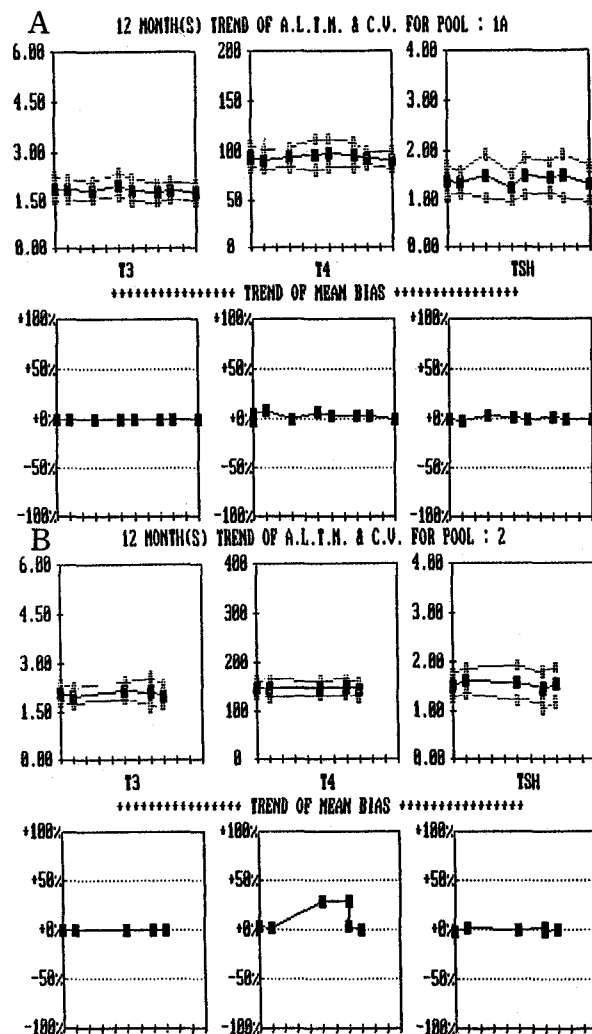

Fig. 4. One of the trends charts of pools from September, 1989 to August, 1990. Every page will show the reproducibility of ALTM of T3, T4 and TSH assay of 11 pools throughout operation. A) This is an example of pool 1A. Ticks on abscissa is each month of the year. B) Another example of the trends chart showing the tidal changes of ALTM, SD and biases. See text for explanation.

the abscissa representing the months of the year (from September of 1989 to August of 1990) should be considered in two halves. One should notice the drift within batch of ALTM's of T3, T4 and TSH in the first and second half of each box respectively, and the drift between halves did mean the between batch drift.

As the 'trends of bias plot' the lower three boxes of the mean of biases for each assay of that pool were listed. In case of pool 2 (Fig. 4B), there was no significant changes of ALTM or SD of T4 concentration, but the bias toward the positive value was found. This phenomenon could be expected when the distribution of assay values of all the laboratories were skewed to positive side. Then, the SD of distribution could be within the expected range but the bias could have significant positive or the negative value. If this skewness aggravated with time lapse, especially resulting in negative bias at later parts of distribution, one would be able to discern the deterioration of that sample (degradation of hormones included in the batches of pool).

3. Interlaboratory Interassay Coefficient Variation (CV)

Interlaboratory interassay (between laboratory between assay) CV's were concentration dependent, higher in the lower values for T3 and T4. Even if it had also the CV over 40%, CV's were less than 20% for most of the T3 assays (Fig. 5A). For low T4, CV's were ranged from the median of 15% to more than 50% (Fig. 5B).

In case of TSH, the situation was somewhat different (Fig. 5C). For the broader range of TSH (1 to 25 mU/L), the interlaboratory interassay CV was not so high. But the CV's rose abruptly and reached the value of 200% when the concentration of the samples was less than 1 mU/L. The CV's of TSH less than 1 mU/L were almost 200%.
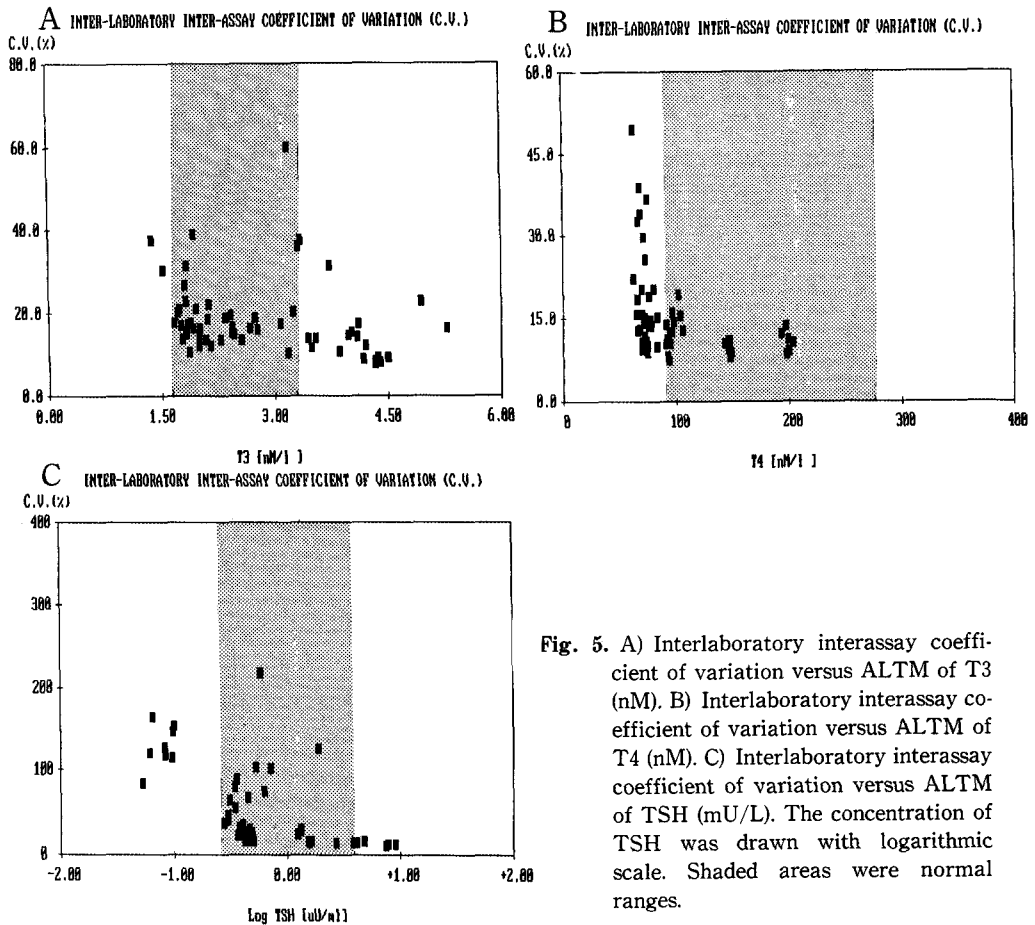
Fig. 5. A) Interlaboratory interassay coefficient of variation versus ALTM of T3 (nM). B) Interlaboratory interassay coefficient of variation versus ALTM of T4 (nM). C) Interlaboratory interassay coefficient of variation versus ALTM of TSH (mU/L). The concentration of TSH was drawn with logarithmic scale. Shaded areas were normal ranges.

Table 8. Recovery of T4, T3 and TSH in the First Year Operation

	Pools	Expected value	Actual value	Recovery (%)
T4*	Pool 2	50 nM	53 nM	106%
	Pool 3	100 nM	104 nM	104%
T3*	Pool 5	1.5 nM	1.0 nM	67%
	Pool 6	3.5 nM	2.6 nM	74%
TSH**	Pool 7A	15 mU/L	13.1 mU/L	87%
	Pool 8A	5 mU/L	4.3 mU/L	86%
	Pool 8B	13.1 mU/L	10.8 mU/L	82%***

  * Pool 1A and 1B : Normal euthyroid, 1A (Bankok), 1B (Lahore)
    Pool 2 : Pool 1A + 50 nmol/L T4,   pool 3 : Pool 1A + 100 nmol/L T4
    Pool 4 : Pool 1B + 1.5 nmol/L T3,   Pool 5 : Pool 1B + 3.5 nmol/L T3
 ** Pool 6 : T3 suppressed (Seoul)
    Pool 7A : Pool 6 + 5 mU/L TSH, Pool 8A : Pool 6 + 15 mU/L TSH
*** Pool 8B : The sum of Pool 6 (T3 suppressed), Pool 7B (TRH stimulated)
        ALTM of Pool 6 : 0.25 mU/L,   ALTM of Pool 7B : 25.9 mU/L

4. Percentage of Outliers in Each Pool[17]

We defined unacceptable performance of one assay based on the degree of bias of individual laboratory in each pool. Outlier was defined as the result of more or less than 3 SD of ALTM. But each laboratory should take the global behavior of all the laboratories in to consideration. So the mean % bias and the variability of the bias should be referred for comparison of each bias.

Mean percentage of outliers of T3, T4 and TSH in each pool were 4%~16%, 1~10%, 3~44%, respectively (Fig. 6). According to the Fig. 6, outliers of T3, T4 and TSH were not distributed among different concentrations (ALTM's). So the appearances of outliers did not seem to depend upon the characteristics of individual batch of pools. The occurrence of outliers could be thought to be caused totally by random noise. Even with the pools of very low level of TSH, the interlaboratory variations were very high, therfore most of the fluctuatung results were within 3 SD and the percentage of outliers did not increase very much.

But, if one laboratory would like to be convinced with the results they have produced, one must consider the 2 SD or 1 SD outliers, too.
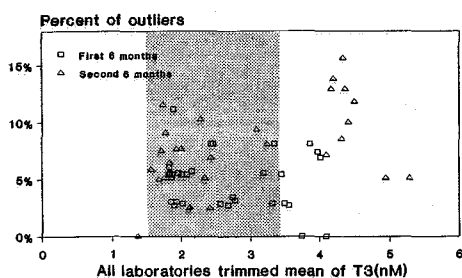
5. Recovery of Hormones

Table 8 is the data of recovery of T4, T3 and TSH. Recovery of hormones were calculated subtracting the mean of the ALTM's of pool 1A or 1B from the means of pool 2 and 3, or 4 and 5, respectively. The expected value for recovery of T4 of pool 2 was 50 nM, and that of pool 3 was 100 nM. The recovery of pool 2 for T4 was 106% of the expected one. The recovery of pool 3 for T4 was 104%.
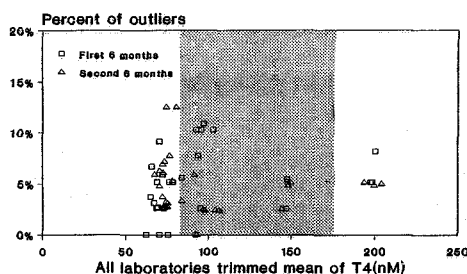
For T3, recovery of hormone of pools 4 and 5 should be 1.5 nM and 3.5 nM respectively. The virtual recovery of T3 of pool 4 was 67%. That of pool 5 was 74%.

For TSH, recovery of pools 7A and 8A should be 5 mU/L and 15 mU/L, respectively. The recovery of pool 7A was 87%, that of pool 8A was 86%. The
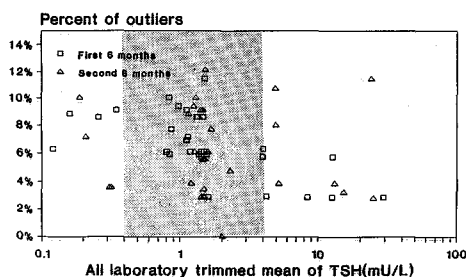

Fig. 6. A) Percent of outliers of each pool. ALTM of T3 (nM) versus percent of outlier. Shaded areas denote normal range. B) ALTM of T4 (nM) versus percent of outlier. C) ALTM of TSH (mU/L) versus percent of outlier. Shaded areas denote normal range.

recovery of 8B was 82%.

6. Data Processing and Reporting

With the algorithm, produced by one of authors (Kwark C), one can handle the data, make out the report forms, and analyze the performances of the individual laboratory and the global trend of performances of all the participating laboratories.

With this program, at first, we do put the data collected via mail to the defined areas of raw data in the program each month. When enough data is available, all laboratories trimmed mean (ALTM) for T3, T4 and TSH is calculated and with the same trimmed data, program calculates the standard deviation (SD) and coefficient of variation (CV) of that sample. Then with the data of all the participating laboratories, program calculates the bias of each laboratory [(data of each laboratoy-ALTM)/ ALTM]. Program calculates the mean and variability of biases of population.

Then, this program goes on to print the report form of data of T3, T4 and TSH of each laboratory. When each laboratory gets the report, they come to know to what their samples belong (because they had been distributed in a blind fashion), and the ALTM (T3, T4, and TSH) of the samples, SD's, CV' s, mean biases, and the actual equivalent values of their own laboratories.

Summary report of laboratories' data for T3, T4 and TSH of samples of each laboratory, ALTM, SD and CV is printed. Three copies for each hormone of these report forms will be given to every laboratory each month (or each term).

With each pool, when all the samples of one batch had been despatched, after all the data were collected, the tidal changes of ALTM, SD and mean bias for each of the hormones (T3, T4 and TSH) are shown. When one wants, one can get the digital data of ALTM and CV beneath the trend graphs of each pool (or batch).

If one operation has finished, the trends of the performances of all the laboratories handling each pool is expressed with three types of graphs or tables. Program gives the tables of outliers for each sample of pool. One can get the graph of outliers (percent: ordinate) versus ALTM (abscissa). Interlaboratory interassay (between laboratory between batch) CV's are plotted against ALTM for T3, T4 and TSH[24].

7. Impact of EQAS Project in Korea

1) The EQAS Project Itself

Three times, the chief technologists of the participating laboratories convened and held the meeting about the EQAS of Korea as part of the meeting of the Korean Society of Nuclear Medicine Technologists. One of authors (Bo Youn Cho) had presented the pros and cons of external quality control in those meetings. They decided to sustain the EQAS of thyroid related hormones, and the number of the participating laboratories increased to 45 for the second year of operation.

Two more items had been included in the external quality control of the second year of operation. They are beta-HCG and alphfetoprotein[16].

It was emphasized that they should receive the results earlier, that is, not after the completion of one term but after the collection of the data for each month. The first year operation of EQAS was not with the pre-prepared data processing package, so the analysis and the making of reports were not possible as required. Now we have software packages to handle so many data and come to be able to report immediately after finishing the analysis each month.

In United Kingdom, which nation has been running the most desirable nationwide external quality control system (UKNEQAS)[19~21], the joining laboratories are numbered over 200, and the reporting service is being done by electronic mail system (E mailage with personal computers)[22]. With these electronic mailing systems, bidirectional communi-

cation would be possible. With the second year of operation, and from now on, the immediate reporting system would play the key role to maintain the nationwide EQAS, to increase the number of joining laboratories and to expand the EQAS to the items that are assayed not very often, but should be quality-controlled externally for the sake of assay and also for the exchange of the reports between laboratories.

It had been suggested that the frequency of external quality control for each of the thyroid hormones should be decreased. It is because of both costs of preparation and costs of assay. Once per two or three months can be considered. Or the alternative is, "Running the EQAS every month, and taking turns of participation". That is to say, every laboratory would participate in the assay and have the duty of reporting every 2 or 3 months in their turns. But the most desirable is that we do the EQAS every month with decreased number of batches. That is, performing EQAS with high, low, and medium concentration of hormones per month for each laboratory.

Each laboratory can handle their data they have received after analysis from center, to find out how their assay for thyroid related hormones performed, and to detect the biases that their assay system would have chances to bear. But these extenal quality control cannot replace the internal quality control that each laboratory should perform.

Because each laboratory do use different radioassay kits perchased from different companies, we are going to analyze our data in a way to disclose the biases of the assay systems of different commercial companies.

2) Prospects

We still have problems that were not agreed upon, "Who will care about the whole procedure?, Who will prepare the EQAS pool batches?, Which items should be included?, and Should every laboratory afford the expenses of EQAS by themselves?" Because most of the laboratories of our country use

the commercial kits for radioimmunoassay, the cost participating in the EQAS is not so small.

In order to solve these problems, the committee for EQAS should be organized in the Korean Society of Nuclear Medicine as well as in the Korean Society of Nuclear Medicien Technologists, and the Societies should cover the costs (manpower and small expenses for center works)[25]. But we think that the costs of assay should be afforded by each participating laboratories, contrary to France where all the finances have been supported by government[23]. And then, if we were not going to burden the costs of assay to the patients, people as the demanders of health care, companies should cover some parts of the costs running the EQAS. If they do cover some of the costs, they can promote the right use of radioassay in our Nation and do contribute the national health care in the real sense.

We think that all these suggestions should be fostered by the organized supports of Korean Society of Nuclear Medicine and Korean Society of Nuclear Medicine Technologists, based upon general agreement among the paricipating members.

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