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**MONGOLIAN  
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## MONGOLIAN JOURNAL OF HEALTH SCIENCES

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# Editorial

Welcome to the new *Mongolian Journal of Health Sciences*.

It is my pleasure to announce beginning with this first volume, the Mongolian Journal of the Health Sciences published by the Health Sciences University of Mongolia twice a year in English and because the progress and achievements of past 60 years of our University are solid foundations for it.

I believe Mongolian Journal of Health Science is a multidisciplinary journal, aiming to cover the whole spectrum of "health sciences". Our goal is to encourage, stimulate and create new ideas and research progresses for the Mongolian health researchers and our colleagues. Also, I believe the single best way to get young researchers involved in the research is to inviting them to publish their work in our journal.

Our journal's mission statement is to provide a means for interchanging ideas among Mongolian health professionals and foreign experts to advance the level of health sciences and promote the cooperation among countries and leading health care institutions. With your help, our journal will have a success.

All of those professionals have a common purpose to promote health sciences and create our new global network since the end of the last century, which is increasing health sciences concepts in various aspects of our life in the world day by day. As shown here, we now reach our first step.

Please do not miss the Mongolian Journal of Health Sciences and the opportunity to subscribe from the beginning.

**Professor Ts. Lkhagwasuren MD., Ph.D., ScD**  
President of Health Sciences University of  
Mongolia  
Editor-in-Chief

# Preliminary comparison of dental occlusion between the Japanese and the Mongolians

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## Abstract

The aim of this study is to elucidate influence of environmental factors on development of the stomatognathic system through occlusal analyses. The parameters of the occlusion of twenty-one Japanese grown on a soft dietary pattern and same number of Mongolians grown on a natural texture dietary pattern were analysed by the pressure sensitive film (Dental Prescale, GC Co. Tokyo, Japan) and the black silicone (Bite Checker, GC Co. Tokyo, Japan). There were significantly differences in the mean occlusal contact area and occlusal pressure, although not difference in the mean occlusal force between the Japanese and Mongolian groups. These finding indicated that the environmental factors could influence several parameters of the occlusion. An analysis of the occlusal contact area is important for the objective evaluation of the prosthodontic treatment according to individual characteristics of people.

**Keywords:** occlusal force, occlusal contact area, black silicone, Dental Prescale, occlusal contact number

## Introduction

**n**

The parameters of occlusion such as occlusal force and occlusal contact area at the intercuspal position (IP) are important for the diagnosis and treatment of the restorative dentistry and the temporomandibular dysfunction. Anthropological researches have shown that the Japanese and the Mongolian populations share genetic similarities<sup>13</sup>, although their dietary patterns are not same. Modern Japanese food is refined and soft, and contains relatively few hard particles. Also it requires little chewing with rather fewer chewing strokes<sup>46</sup>. Mongolia's nutritional structures remain untouched, compared with the other countries such as Japan, although its customs and lifestyles have changed through the onset of industrialization and information technology. The Mongolian basic diet consists of animal husbandry products like meat and dairy products including dried curd. Also, the Mongolians reported to have robust jawbone and developed masseteric tuberosity". It suggests

effective muscle function and occlusal force. The

purpose of this study was to evaluate the influence of environmental factors such as dietary pattern on the development of the stomatognathic system through occlusal analyses.

## Materials and Methods

Forty-two clinically healthy subjects with complete dentitions were recruited for this study. The subjects were divided into two groups 1) Japanese group: 11 female and 10 male Japanese grown on a relatively soft diet (living in Tokyo, Japan) and 2) Mongolian group: 14 female and 7 male Mongolians grown on a more or less natural texture diet (living in Ulaanbaatar, Mongolia). Participants were aware of the objectives of this study. The subjects were limited between 18-30 years of age (mean age 23.8±3.4 yrs) to minimize the tooth wear associated with age. Dental impressions were taken with alginate for all participants and dental casts prepared.

**Dental Prescale measurement**

The subjects were instructed to bite on pressure-sensitive sheets Dental Prescale (Type-R50H, Fuji Film Co., Tokyo, Japan.) for analyses of the occlusal contact area (mm<sup>2</sup>), occlusal force (N), and occlusal pressure (MPa). The thickness of pressure-sensitive sheet was about 100 um. All measurements were made at the intercuspal position during the maximum clenching. The three trials of Dental Prescale measurements were performed for each individual to augment reliability and reproducibility and the mean value of three measurements was used. The validity of Prescale has been evaluated in previous studies<sup>78</sup>. An image scanner (Dental Occlusion Pressuregraph FPD-703> Fuji Film Co., Tokyo, Japan.) measured coloration density and converted this to a pressure scale. The data were transferred to a personal computer (Apple Computer Inc., CA, USA.) and then were processed by analysing software (Occluzergraph-M Ver. 1.0, Fuji Film Co., Tokyo, Japan.).

**Black silicone measurement**

Black silicone records (Bite Checker, GC Co., Tokyo, Japan.) were taken from the subjects for analyses of the occlusal contact area (mm<sup>2</sup>) and number. Since black silicone increases in opacity with its increasing thickness, perforations or translucent areas with clearances as great 30 um were represented as occlusal contacts according as previously described by Nakao<sup>9</sup>. The records were placed on the light source for luminance of occlusal area, onto which a photo camera (Nikon. Co, Tokyo, Japan.) focused with calibrated height and shutter speed to take image. The images of black silicone record were digitised and analysed by using software (WinROOF Ver.3.03,Mitam.Co, Tokyo, Japan.) to a personal computer. To standardize the procedure, the one operator recorded data for all measurements. The Student's t-test was used for statistical analysis. Levels of P<0.05 were considered to be statistically significant.

**Results**

The parameters of the occlusion measured by the Dental Prescale system are shown in the Table 1. The mean occlusal contact area of the Japanese group was significantly smaller (P<0.05) than that of the Mongolian group. Also, the occlusal contact area was statistically significant different (P<0.01) between the females of both groups. There was not significant difference in the mean occlusal force between the Japanese and Mongolian groups (P<0.05). The mean occlusal pressure of the Japanese group was significantly

**Table 1.** The parameters occlusion measured by Dental Prescale .

		Occlusal contact area (mm <sup>2</sup> )	Occlusal Force (N)	Biting pressure (MPa)
Japanese	Total (21)	22.5 ±8.5	906 ±278	41.4 ±5.4
	Male (10)	25.2 ±11.0	975 ±348	40.4 ±6.7
	Female(11)	19.8 ±3.9	836 ±176	42.4 ±4.0
Mongolian	Total (21)	29.2 ±10.3	1022 ±309	36.7 ±4.8
	Male (7)	33.3 ±7.3	1109 ±449	35.5 ±5.3
	Female(14)	27.0 ±10.3	975 ±309	37.4 ±4.8

Data are expressed as the mean ±s.d. The number of subjects given in parentheses. Level of significant difference: \* P<0.05, \*\* P<0.01( unpaired t-test) .

**Table 2.** The occlusal contact area and number measured by black silicone .

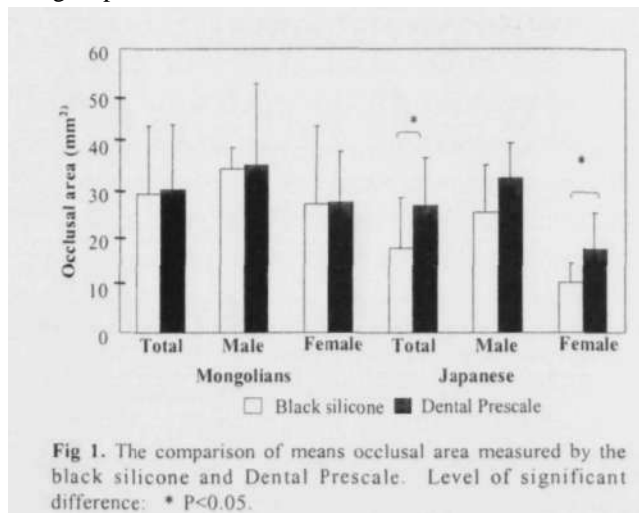
		Occlusal contact area (mm <sup>2</sup> )	Occlusal contact number
Japanese	Total (n=21)	18.0 ±10.5	26.0 ±9.7
	Male (n=10)	25.3 ±9.9	31.5 ±9.1
	Female(n=11)	10.7 ±4.0	20.4 ±6.9
Mongolian	Total (n=21)	30.0 ±13.4	31.3 ±9.4
	Male (n=7)	36.0 ±6.7	37.2 ±6.0
	Female(n=14)	27.2 ±15.0	27.8 ±10.0

Data are expressed as the mean ±s.d. The number of subjects given in parentheses. Level of significant difference: \* P<0.05, \*\* P<0.01( unpaired t-test) .

higher (P<0.01) than that of the Mongolian group. In the Japanese female, the occlusal pressure was higher than those of the other three subject groups. The mean occlusal contact area and occlusal contact number measured by the black silicone method are shown in the Table 2. The mean occlusal contact area showed statistically significant difference (P<0.01) between the Japanese and Mongolian groups. The mean number of occlusal contact of Mongolian female group was significantly more (P<0.01) than that of the Japanese female.

A comparison of mean occlusal contact area measured by the black silicone and Dental Prescale

system is presented in Fig. 1. A significant difference ( $P < 0.05$ ) was observed on the data measured between the two methods in the Japanese group.



### Discussion

We examined whether there are any differences in occlusal contact area, occlusal force and occlusal pressure between the Mongolian and the Japanese group according to their dietary patterns. Also this study was first attempt to investigate the parameters of the occlusion of the Mongolian population.

In this study, the subjects were consistently suggested to perform the maximum clenching at the intercuspal position as described in previous studies<sup>710</sup>. Also we eliminated the possible factor of data error by comparing the colored sites on the pressure-sensitive sheet with the black silicone records and dental casts.

According to Tumen<sup>1</sup>, the Mongolians have robust jawbone and developed masseteric tuberosity. Therefore, strong occlusal force might be expected due to their dietary pattern. However, the mean occlusal forces measured in this study indicated that there were not significant differences between the two groups. The occlusal force of both groups was similar to the findings in the Japanese population<sup>7-810</sup>. This is in agreement that hard food do not induce stronger muscle force to break and chew the food, instead require longer muscle contraction time with relatively unchanged occlusal force<sup>6</sup>.

The mean occlusal contact area in the Mongolian group was significantly larger than that

of the Japanese group. The occlusal force was the same magnitude in both groups, the difference in occlusal area could attribute to the attrition possibly caused from the dietary pattern in the Mongolian group. However, the attrition only involving enamel in the Mongolian group was too subtle or moderate to be classified with any wear indices existing currently<sup>1213</sup>. Also, the subjects were limited between 18-30 years of age to minimize tooth wear associated with advancing age. On the other hand, when eating a modern diet, the amount of contact occurring between the teeth is probably insufficient to cause attrition<sup>1416</sup> in the Japanese group.

Regarding the comparison of occlusal contact area measured by the black silicone and Dental Prescale methods, a significant difference was found between the two methods in the Japanese group. The black silicone method is not believed to affect intercuspal position because it can be perforated at the tooth contacts. The gliding contact between opposing unworn occlusal surfaces of the teeth with tendency of the tooth displacement from apical to apicopalatal direction with increase of clenching intensity<sup>1718</sup> could give a larger area of measurement by relatively thick pressure-sensitive sheet of Dental Prescale (100um) in the Japanese group. However, in the Mongolian group with the tooth displacement along to the tooth axis<sup>517</sup>, the occlusal contact area did not appear to generate difference between the black silicone and Dental Prescale methods.

In the present study, the mean occlusal contact area of the Mongolian group was significantly larger than that of the Japanese group. There was not significant difference in the mean occlusal force between the Japanese and Mongolian groups. The mean occlusal pressure of the Japanese group was significantly higher than that of the Mongolian group. These finding indicated that the environmental factors could influence several parameters of the occlusion and analysis of the occlusal contact area. The difference on the occlusal area attributed to environmental factor such as dietary pattern is important for objective evaluation of prosthodontic treatment according to individual characteristics of people.



### Conclusion

1. The mean occlusal contact area of the Mongolian group was significantly larger than that of the Japanese group by both methods.

2. There was not significant difference in the mean occlusal force between the Japanese and Mongolian groups.

3. Environmental factors can influence several parameters of the occlusion.

4. Analysis of the occlusal contact area distribution over dentition is important for objective evaluation of prosthodontic treatment according to individual characteristics of people.

*The essentials of this article were reported at the 22<sup>nd</sup> Asian Pacific Dental Congress and 19<sup>th</sup> General Meeting of Japanese Association for Dental Science, Tokyo, Japan, May 2000.*

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## The study of mitochondrial DNA control region in Mongolians

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### Abstract

Sequencing results of the mitochondrial DNA control region for 100 Mongolians are presented. Sequences of 340 nucleotides for hypervariable region I were analysed. 61 polymorphic sites and 51 different haplotypes were determined. Genetic substructuring was lower comparing to the results of other studies for Asian populations. It could be useful to determine sequence polymorphisms for Mongolian ethnic minority groups in order to describe their demographic history and ethnogenesis.

**Key words:** Mitochondrial DNA, polymorphic sites, Mongolians,

### Introduction

The Human Genome Project, from one perspective began in 1981 with the publication of the human mitochondrial DNA (mtDNA) sequence. The human mtDNA is a double-stranded, circular molecule of 16 569 bp and contains 37 genes coding for two rRNAs, 22 tRNAs and 13 polypeptides. Mitochondrial DNA is distinct from nuclear DNA. Firstly, the evolutionary rate of nucleotide substitution is higher than in nuclear DNA. Secondly, mtDNA is maternally inherited, which means no recombination is involved. Thirdly, they contain 1.1 kb-long (7%) control region, which shows severe polymorphism. Fourthly, they exist in cytoplasm with numerous copy numbers<sup>14</sup>. Therefore, mtDNA seemed to be a possible subject of evolutionary studies and a valuable tool in individual identification

This study presents the sequencing data for the mtDNA control region in 100 Mongolians.

### Materials and methods

#### 1. DNA extraction

100 blood samples from Mongolian nationals were collected at Seoul National University Medical College. Total genomic DNA was extracted from blood using phenol-chloroform method with proteinase K.

#### 2. Amplification and sequencing

The amplification of the mtDNA control region was carried out from 50ng of genomic DNA using primers as follows: F: GAT GTC TGT GTG GAA AGT GG, R: CCT CAT CCT AGC AAT AAT CC. The result of amplification was confirmed by electrophoresis in 1% agarose gel.

After purification and elution, the amplified region was used for sequencing.

We aligned and compared our sequences using "Bioedit sequence alignment editor" version 5 0.9 program.

### Results and discussion

Average molecular weight (D) of sequenced nucleotides was 207116.5, average identity to Anderson's reference sequence - 0.9667, average adenine content - 34.3995% , average thymine content - 25.5737%), average guanine content - 13.2196%, average cytosine content - 26.6073% .

61 polymorphic sites (compared to Anderson's data) were noted: 374 transitions (A-G, G-A, T-C, C-T), 103 transversions (G-T, G-C, A-T, A-C, T-G, T-A, C-G, C-A), 6 insertions and 17 deletions.

The nucleotide substitutions commonly noted in Mongolians were found at four sites: at 15932 nucleotide substitution from C to T (in 100% of Mongolians), at 16172 from C to T (in 92%), at

16183 from C to A (in 85%), at 16189 C to T (in 69%).

Fifty one haplotypes were detected, from which 38 were unique, one haplotype was shared by 33 people, another one was shared by 5 people, five haplotypes were shared by 3 people and six haplotypes were shared by 5 individuals.

The haplotype diversity (h) of Mongolian mtDNA was 0.939 and nucleotide diversity (n) was 0.017. Genetic substructure was lower comparing to the results of other studies for Asian populations. Our data is rather similar to that of Korean and Tibetan<sup>5</sup>. (Table 1)

As the next step of our study it could be valuable to determine sequence polymorphisms for Mongolian ethnic minority groups in order to

describe their demographic history and ethnogenesis.

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*Table 1*  
Haplotype diversity (h) and nucleotide diversity (n) of mtDNA in Asian populations.

Nationality	Number of subjects	Haplotype diversity	Nucleotide diversity
Mongolians (our data)	100	0.939	0.017
Tibetians(Yao, 2001)	40	0.933	0.013
Koreans (Lee, 1997)	306	0.930	N/A
Han (Tsai, 2000)	52	0.993	0.019
Tai(Yao, 2001)	32	0.994	0.020
Japanese (Seo, 1998)	100	0.999	N/A

## **The attitude, knowledge and needs of adolescents on sexual and reproductive health among adolescents from secondary schools, Ulaanbaatar city**

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The purpose of this study was to evaluate Sexual and Reproductive Health knowledge, attitude and needs of a number of adolescents of age 14-18 and school teachers from secondary schools of Ulaanbaatar city. To assess knowledge, attitude, needs on Sexual and Reproductive Health through Focus group Discussion and specially worked Multiple Choice Questionnaire (MCQ) among the adolescents and school teachers. The MCQ was conducted among 510 randomly selected school children (285 girls and 225 boys) aged 13-18 from selected schools #13, 40, 86, and 93 from Ulaanbaatar city. Baseline data was collected with respect to adolescents knowledge of RH using a pre-test questionnaire with comprised about 29 set of MCQ about contraception, problem between girlfriends and boyfriends, sex, media education, STIs, HIV/AIDS, tobacco and alcohol. Most of the adolescents have very insufficient knowledge on contraceptives. 74.7% of girls has knowledge on condoms, while this rate is 92.5% in boys. 56.8% of girls and 66.4% of boys gave "YES" answering the question "Can teenagers use contraceptive methods?" that demonstrates that they have poor knowledge on this matter. Although 90% of adolescents have heard of STIs, they have no sufficient knowledge on their symptoms. 52% out of total number of adolescents know about gonorrhoea, 30% of them know about trichomoniasis, 20.5% know about syphilis and 96% know about HIV/AIDS. 79% of the participants of the survey have answered that they have extreme need in information on family planning, pregnancy, contraceptives, STIs and HIV/AIDS which demonstrates big need in this kind of information. Adolescents have a great need in RH information, most of them do not know where to get this kind of information, and source of such information is not available for some of them. For some of them the received information is not sufficient and does not meet needs of adolescents. Most of participants of the survey agree that RH information is insufficient.

**Key words:** sexual and reproductive health, STI, HIV/AIDS

### **Introduction**

Adolescence is the transition from childhood to adulthood, marked by profound physical, emotional, mental and social changes. We define adolescence as the time period from ages 10 to 24. We use the terms "adolescents", "youth", "young adults" and "young people" interchangeably. In such a broad range, reproductive health needs can vary greatly. The needs of a 10-year-old who has not yet reached puberty and who is not sexually active will be considerably different from those of an 18-year-old who is newly married, or a 24-year-old with two children.

Change is the hallmark of adolescence. Physical changes, such as growth of facial hair for boys and onset of menstruation for girls, take during puberty, which occurs mostly from ages nine to 14 boys and ages eight to 13 for girls.

As adolescents become adults, they consider sexual relations, marriage and parenthood as signs of maturity. They seek information and clues about sexual life from a variety of sources-parents, peers, religious leaders, health providers, teachers, magazines, books mass media. While youth receive a wealth of information from diverse sources, a

good deal of that information is incorrect, incomplete or misleading.

Counseling is critical for all reproductive health clients, including adolescents. The goal of counseling is to provide young people with facts that will enable them to make informed, voluntary decisions. Reproductive health worker should offer information and guidance, but ultimately, the adolescent must decide whether he or she needs a contraceptive method that also offers sexually transmitted infections (STI) protection, or whether to seek STI treatment. . The purpose of this study was to evaluate Sexual and Reproductive Health knowledge, attitude and needs of a number of adolescents of age 14-18 and school teachers from secondary schools of Ulaanbaatar city.

**Materials and Methods**

To assess knowledge, attitude, needs on sexual and reproductive health through focus group discussion and specially worked multiple choice questionnaire among the adolescents and school teachers.

*Activities*

Focus group discussions (FGD) were held in every schools with school children and informal discussions were held with teachers. A total of 4 Focus group discussions were conducted.

Girls and boys of each school proposed to have FGD together, not separately for girls and boys.

The selected adolescents had an almost similar socio-economic status. In each group 6 participants were invited and on the guidelines were the different elements of sexual issue and reproductive health and average 6-8 participants were actually present per session. They have poor and lack of knowledge and attitude and need of correct information on STDs, contraceptives and sexual education.

*A pre-test questionnaire of Multiple Choice Questions (MCQ)*

The MCQ was conducted among 510 randomly selected school children (285 girls and 225 boys) aged 13-18 from selected schools#13,40, 86, and 93 (Table 1).

**Table 1. Total number of participants**

Age	Boys		Girls	
	Frequency	Percent	Frequency	Percent
13-14	62	27.4%	31	10.9%
15-16	145	64.2%	146	51.2%
17-18	18	8.4%	108	37.9%
<b>Total</b>	<b>225</b>	<b>100%</b>	<b>285</b>	<b>100%</b>

Baseline data was collected with respect to adolescent's knowledge of RH using a pre-test questionnaire with comprised about 29 set of MCQ about contraception, problem between girlfriends and boyfriends, sex, media education, STIs, HIV/AIDS, tobacco and alcohol. All indices were processed with use of SPSS 10.0 program.

**Results**

Total number of adolescents who participated in pre-test questionnaire of Multiple-choice questions was 510.

The table 2 demonstrates way how adolescents get information on contraceptives, sexual relations and need in it. 94-96% of adolescents answered "YES" the question "Do you know any contraceptive method?" But when they were asked in detail, it was revealed that most of them have very insufficient knowledge on contraceptives.

74.7% of girls have knowledge on condoms, while this rate is 92.5% in boys. 56.8% of girls and 66.4% of boys gave "YES" answering the question "Can teenagers use contraceptive methods?" That demonstrates that they have poor knowledge on this matter.

Table 3 demonstrates that 35% of boys consider that it is "OK" to have sexual relations at age 18-19 that 36% of girls consider to have sexual relations after marriage.

45.6% of boys aged 14-18 had sexual relations and that most of them (64.8%) had their first sexual relations at age 15-16 (Table 4).

**Table 2. Knowledge on contraceptives**

	Do you know any contraceptive method?	Can adolescent use contracep-tives?	IUD	Calendar	Depo-Drovera	Condom	Norplant
	Yes	Can					
Boys	96%	66.4%	10.6%	10.2%	11%	92.5%	6.6%
Girls	94%	56.8%	13.7%	22.5%	8.4%	74.7%	3.5%

Table 3. Concerning sexual relations

Age	What age in can be sexual relations?											
	14-15		16-17		18-19		20-23		After marriage		No idea	
Boys	22	9.7%	45	19.9%	81	35.5%	25	11.1%	16	7.1%	31	13.7
Girls	2	7%	-	-	68	23.5	86	30.2%	104	36%	16	5.6%

33.2% of boys and 62.5% of girls that had sexual relations worry about danger to be infected by STIs,

32.7% of boys and 70.5% of girls are afraid of becoming pregnant.

Table 4. Knowledge on sexual relation

	Is it possible for girls and boys to abstain from sexual relations?				Have you had sexual relations?	
	Yes	No	Depending on situation	No idea	Yes	No
Boys	51.6%	4%	36.3%	8.4%	45.6%	54.4%
Girls	54.7%	1.4%	20.4%	15.1%	6.3%	93.7%

31% of boys use any of contraceptive methods during sexual relations, while 74% of boys and 39.4% of girls use a condom.

Although most of adolescents have heard of STIs, they have no sufficient knowledge on their symptoms. 52% out of total number of adolescents know about gonorrhoea, 30% of them know about trichomoniasis, 20.5% know about syphilis and 96% know about HIV/AIDS (Table 5,6).

Table 5. Knowledge on STIs and AIDS

	Have you heard about STDs?		Do you know symptoms of STDs?		
	Yes	No	Yes	Not much	No
Boys	89.8%	10.2%	23.9%	33.2	38.5
Girls	90.9%	9.1%	14.1%	42.8	42.1

## Discussion

The participants of the survey have also answered that the main sources of the above information are TV (64.9%), press (42%) and friends (25%).

Table 6. Information on FP, sexual education. STIs and HIV/AIDS

	Sufficiency of information on family planning, pregnancy, sexual education. STIs, HIV/AIDS	
	Sufficient	Insufficient
Boys	30.1%	64.6%
Girls	26.3%	71.0%

79% of the participants of the survey have answered that they have extreme need in information on family planning, pregnancy, contraceptives, STIs and HIV/AIDS that demonstrates big need in this kind of information.

The fact, that they consider parents (3%), teachers and school (1%) as source for information

on STIs and HIV/AIDS, demonstrates that, although health classes are included in school academic curriculum, it could not become efficient source for reproductive health and that parents have very poor knowledge of this kind of information and cannot have close and open talk with their children.

The above dates demonstrate that very little attention is paid on adolescent health education within family and school. It is obvious that the source that they use most of all (friends - 34.2%) is not reliable and provides misinformation.

90% of the participants of the survey have stressed out necessity of a special center where adolescents can get information, consultation and service on adolescent reproductive health and STIs. Caution that their private secret may not be strictly kept and a wrong rumor may be spread out about them makes adolescents to refuse the current health service.

71% out of teachers who teach reproductive health classes are ashamed to talk to adolescents on human anatomy, friendship and sex, and they explained that they face difficulties due to insufficient training that gives just orientation on STIs, HIV/AIDS and reproductive health. Teachers have also stressed the necessity for adolescents to have medical examination and functioning of school based consulting rooms for them (85%) and operation of professional organizations to give consultation by phone (95%).

The fact that most of the participants of the survey accept establishment of RH consulting rooms at schools and phone consulting service with much appreciation shows need in reliable professional organizations able to provide appropriate and correct information.

## Conclusion

1. Although adolescents have a great need in RH information, most of them do not know where to get this kind of information, and source of such information is not available for some of them. For

some of them the received information is not sufficient and does not meet needs of adolescents. Most of participants of the survey agree that RH information is insufficient.

2. Besides need to improve quality of RH classes included in the school academic curriculum, there is need to increase possibility to accept wide-ranged information on adolescent reproductive health in pleasant and appropriate conditions.

3. 90% of the participants of the survey have stressed out necessity of a special center where adolescents can get information, consultation and service on adolescent reproductive health and STIs. Caution that their private secret may not be strictly kept and a wrong rumor may be spread out about them makes adolescents to refuse the current health service.

4. Talk with school teachers who teach RH classes and school doctors has revealed that they

have insufficient information on reproductive health, severe shortage of books, manuals and other materials and are ashamed to talks on these subjects to schoolchildren.

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## Rhenium-188-HDD-lipiodol in treatment of inoperable primary hepatocellular carcinoma

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### Abstract

This paper describes the results of a Phase I study conducted by the International Atomic Energy Agency (IAEA) to determine the safety of trans-arterial Re-188 Lipiodol (radio conjugate) in the treatment of patients with inoperable hepatocellular carcinoma (HCC). Adjuvant intra-arterial radioconjugate therapy could potentially reduce the rate of local recurrence and increase disease-free and overall survival. Rhenium-188 Lipiodol conjugate was prepared using a HDD (4-hexadecyl 1-2, 9, 9-tetramethyl-4, 7-diaza-1, 10-decanethiol) kit developed in Korea, and Lipiodol. 18 patients received one treatment of radioconjugate. The level of radio-conjugate administered was based on radiation-absorbed dose to critical normal organs, calculated following a "scout" dose. The organs at greatest risk for radiation toxicity were liver, lung and bone marrow. A specially designed EXCEL Spreadsheet was used to determine maximum tolerated dose (MTD), defined as the amount of radioactivity calculated to deliver no more than 12 Gy to lungs or 30 Gy to liver or 1.5 Gy to bone marrow. These doses have been found to be safe in multiple trials using external beam therapy and systemically administered radiopharmaceuticals. Patients were followed for at least twelve weeks after therapy, until recovery from all toxicity. The clinical parameters which were evaluated included toxicity; response as determined by contrast-enhanced CT; palliation of symptoms, and overall survival at six months; and quality of life parameters, including performance status (Karnofsky) and hepatic function (Child's classification). All 18 patients had both the "scout" dose and the treatment dose. In the majority of patients, from the "scout" dose studies, the radiation absorbed dose to normal liver was the limiting factor to the treatment dose, where the MTD was determined by the radiation dose to liver, or by dose to lung. Radiation dose to bone marrow was negligible and was thus not a factor for the MTD calculations. Side effects were minimal and usually presented as right hypochondrial discomfort and low-grade fever. Liver function tests at 24 and 72 hours showed no significant changes and complete blood counts at one week, four weeks and 12 weeks showed no changes (no bone-marrow suppression). The results of this Phase I study show that Rhenium-188 Lipiodol is a safe and cost-effective radiopharmaceutical for treatment of primary HCC via the transarterial route, and the new therapeutic procedures should be subjected to further evaluation to determine its efficacy.

**Key words:** Rhenium-188 Lipiodol, hepatocellular carcinoma, scout dose

### Introduction

Hepatocellular carcinoma (HCC) is one of the most common malignant tumors in Mongolia. It is a common malignancy worldwide, causing almost

one million deaths annually<sup>5</sup>. Asia is a high-risk area, the disease being particularly highly prevalent in China, Vietnam, Japan, Mongolia, Singapore and Korea<sup>6</sup>.



The main risk factors for HCC are cirrhosis, persistent hepatitis B virus (HBV) and C virus (HCV) infections. Other associated factors in the causation of HCC are also toxins, hepatic venous outflow tract obstruction, alcohol and smoking<sup>7</sup>.

Patients with HCC have a poor prognosis, with a 5-year survival rate of less than 5%. A median survival rate of less than 4 months for patients with unresectable HCC has been reported<sup>8-9</sup>. Surgical resection is possible only in a minority of patients, since most patients present with advanced disease. Following curative resection, early recurrence of HCC is common<sup>7</sup>. Other forms of treatment include orthotopic liver transplantation (OLT), percutaneous ethanol, acetic acid or hot saline injection, microwave and laser treatment, external radiation, systemic chemotherapy, transarterial chemoembolisation (TACE), and transarterial oily chemoembolisation (TOCE). Side effects are associated with chemoembolisation, and the result is not very encouraging<sup>10</sup>.

Uncontrolled studies using radionuclides such as Iodine-131, Yttrium-90 (microspheres), Holmium-166 and Rhenium-186 conjugated to monoclonal antibodies, lipiodol or chemical compound have produced fair results<sup>11,12</sup> but their efficacy has to be optimally evaluated. For unresectable HCC, hepatic trans-arterial radioconjugate aim to deliver high radiation dose to the tumor, but at the same time limiting the radiation to normal liver, lung and bone marrow to within maximum tolerated dose (MTD). This approach is possible because the blood supply to HCC is mainly from the hepatic artery, while normal liver parenchyma obtains 80% of the blood supply from the portal vein. Lipiodol localises in hepatic tumors when administered via the hepatic artery.

In this paper we present our initial experience with a new radio-conjugate, namely Rhenium-188 HDD Lipiodol (Re-188 Lipiodol). The objectives of this study were to establish the safety of transarterial Re-188 Lipiodol in patients with inoperable HCC, establish MTD to normal liver, lung and bone marrow and determine the adverse effect and response rate for this radiocojugate treatment in a small group of patients.

## Materials and Methods

### *Radio-conjugate*

Rhenium-188 is radionuclide with a physical half-life of 16,9 hours. It emits b-rays that are energetic and potential cytotoxic with a mean energy of 795 KeV, and y-rays with energy of 155 KeV in 15% abundance. Thus, gamma-camera imaging for biodistribution studies is possible. Re-188 is eluted from a tungsten-188/rhenium-188 generator (Oak Ridge National Laboratory, Oak Ridge, USA), which has a long useful shelf-life of several months, and provides a good yield of carrier-free Rhenium-188 on routine basis<sup>12</sup>.

The 4-hexadecyl 1-2, 9, 9-tetramethyl-4, 7-diaza-1,10-decanethiol (HDD) lyophilized kits were obtained from Seoul National University Hospital, Korea. Briefly, the concentrated eluate from the Tungsten-Rhenium generator is heated with the HDD in a water bath for 1 hour to produce Re-HDD complex. Lipiodol is then added and centrifuged to extract the Re-HDD into the Lipiodol. The Re-188 HDD Lipiodol radioconjugate is stable for at least 4 hours. Routine Quality Control for radiochemical purity was done in all cases prior to patient injection.

### *Patient Selection*

The Ethics Committee of the University approved the use of Re-188 Lipiodol for the treatment of unresectable HCC on compassionate grounds. Patients were informed of the potential risk of hepatic angiography and proposed radioconjugate treatment and consents were obtained. The patients were informed the potential benefits of therapy, which included improved quality of life, tumor response and suppression of disease progression. HCC was diagnosed in this population by histopathology or clinically in patients who had consistently (over 15 days or longer) elevated levels of serum alpha-fetoprotein (>500 ng/ml) and space occupying lesion(s) in liver on CT consistent with HCC.

### *Eligibility Criteria*

1. Patients must be at least 18 years of age;
2. Patients must have bi-dimensionally measurable disease by computed tomography, which must demonstrate a solitary lesion (>5 cm in greatest diameter), or <3 lesions (<3 cm in greatest

diameter), or an inoperable solitary lesion of less than 8 cm in greatest diameter; 3. All patients must have discontinued their chemotherapy or immunotherapy for at least 4 weeks, and bronchodilators and/or steroids for at least 8 weeks prior to entry into the study; 4. Female patients of childbearing age were required to have a negative pregnancy test carried out on the day of and prior to study entry, and must be asked to use effective contraception during the study period of 12 weeks; 5. All patients must be ambulatory with a Karnofsky status of  $\geq 70\%$ ; 6. Serum creatinine  $\leq 2\text{mg/dL}$ ; 7. ANC  $\geq 1,500/\text{microL}$ , platelet count  $\geq 100,000/\text{microL}$ ; 8. Prothrombin time  $< 1.3 \times$  control, and/or INR  $< 1.5$ ; and 9. Patients must have signed an Informed Consent form for participation in this study.

#### *Exclusion Criteria*

1. Patient with Child's C status (Table-1); 2. Clinically significant cardiac disease class III/IV (New York Heart Association); 3. Pulmonary disease, e.g. asthma/COPD, requiring bronchodilators; 4. FEV1/diffusion capacity  $< 70\%$  of normal; 5. Serious infection requiring antibiotic treatment, or other serious illness; 6. Pregnancy or lactation; 7. Survival expectancy of less than 1 month; 8. Evidence of extra-hepatic spread; 9. Allergy to intravenous contrast; 10. Patients with ruptured HCC.

#### *Administration of radio-conjugate*

Patients were admitted for hepatic angiography and treatment after extent of disease and related studies confirmed eligibility, and consents obtained. CT scans of liver were obtained when the patients were in the ward, to assess pre-treatment size of tumor and also to assess liver and tumor volume(s) for the gamma-camera dosimetry studies next day. The day before the treatment the patients were sent to Nuclear Medicine Department for flood source transmission scans to obtain attenuation correction factors for lung and liver, for use in the dosimetry calculation the following day. An interventional radiologist performed hepatic angiography via a femoral puncture, on the day of treatment. The transarterial infusion of radioconjugate was done in as selective a manner as possible and as close to the feeding artery as

possible. The initial infusion or "scout" dose was about 200 MBq, carried out slowly over a period of 5 minutes, taking care not to reflux the radioconjugate into the gastroduodenal artery to minimize risk of radiation gastritis. If there were multiple tumors, the dose was administered in approximately equal volumes via the arteries supplying the two largest tumors.

With the catheter in place in the feeding artery, the patients were transported to the Nuclear Medicine Department. Imaging of the "scout" dose in the liver was performed in static mode over liver and lung. Whole body scans were also done in the first 6 patients. Both anterior and posterior images were obtained to calculate the geometric mean of counts. Regions of interest (ROI's) were placed over lung, liver and tumor, and counts per pixel obtained (geometric means) to calculate MTD to liver and lung, using an EXCEL Spreadsheet<sup>18</sup>. The first 5 patients also had plasma radioactivity measured to assess bone-marrow dose, but since this dose was found to be negligible, blood samples were abandoned.

Following the scout dose imaging and dosimetry studies, the patients were sent back to the Radiology Department (Angiography suite) to ensure no change in catheter position and for injection of the calculated treatment dose, usually within an hour of the scout dose. Patients were sent back to their isolation-rooms in the ward and monitored for symptom/adverse effects and biochemical abnormalities. Patients were discharged usually on the third or fourth day after admission. Therapy dose analyses were also abandoned after the first few patients, since the gamma-camera dosimetry with large doses was unreliable (underestimated) compared to the 'scout' doses.

#### *Post-Treatment Evaluation*

A successful course of therapy was defined as completion of one therapeutic administration of radioconjugate. End of therapy was defined as 12 weeks after administration of therapeutic dose of Re-188 Lipiodol. End of study was defined as death; or one year after end of therapy. Progression of diseases was defined as: increase in number of lesions, or extra-hepatic spread, or decrease in Child's status to C or worsening of Karnofsky status.

*Response Parameters*

CT measured extent of disease not more than 2 weeks before study entry, and between 6 to 8 weeks after therapy. Response was evaluated using the same imaging methodology as used for estimation of the pre-treatment extent of disease. Patients were seen at quarterly intervals after the end of therapy, until end of study or death, whichever was earlier?

Where possible, response parameters were classified as follows:

1. Complete response: Disappearance of all measurable disease.
2. Partial response: Fifty percent or greater reduction in size of the product of 2 perpendicular diameters of any measurable lesion and no new lesion.
3. Stable Disease: No change in the size of lesions; a decrease in size of lesions but less than a partial response; no new lesions.
4. Mixed Response: Increase in size of some lesions, and decrease in size of other lesions, with/without appearance of new lesions.
5. Progression: Appearance of new lesions, or increase by 25% or more in size of any measurable lesion
6. Response Duration: Duration is measured from the start of treatment until progression.

*Toxicity*

Toxicity was graded in accordance with the Common Toxicity Scale developed by the National Cancer Institute of the USA.

*Adverse Events*

An adverse event was defined as any new undesirable medical experience or change of an existing condition that occurred during or after administration of an investigational agent, whether or not it was considered agent-related. Abnormal laboratory findings considered to be clinically significant were also considered adverse events.

Table 2. Summary of results in 18 patients

Adverse effects\ toxicity	Nausea 2	Nausea and Vomiting 1	Low - grade Fever 8	Right hypochondrial discomfort 6
Tumor size Reduction	No change 12	10 - 25 % reduction 4	50% Reduction 2	
Quality of Life	Improvement 5	No change 13		
Status	Alive at three months 17	Alive at six months 15		
Response	Stable 16	Partial 1	Progression 2	

**Results**

The results are shown in table 1 and 2. Eighteen HCC patients had a dosimetry scout dose followed by the therapy dose. The mean scout dose was 210 MBq and mean treatment dose was 4 GBq, making a total mean liver dose of 4,2 GBq Re-188 Lipiodol, after calculations for loss of activity (dose) in syringes and catheters (typically about 5% loss).

The activity concentration in a blood sample was converted to red marrow activity concentration and then total marrow activity using the Standard Man anthropomorphic models. Cumulated activities were calculated assuming elimination of activity only by physical decay in situ. The absorbed doses to the therapy-limiting normal tissues, liver, lung and red marrow, were calculated using the MIRDO schema, adjusting the pertinent S factors for differences in total body and organ masses between the patient and the anthropomorphic model and including the dose contribution from the liver tumors. Finally, based on maximum tolerated absorbed doses of 30 Gy, 12 Gy, and 1,5 Gy to liver, lung, and

Table 1. Patients with scout and treatment dose and Maximum Tolerated Dose limiting organ

No of Patients with scout dose and treatment	Amount of Scout dose mean (range)	Treatment dose mean (range)	MTD Limiting organs
18	210 MBq (141 10 289 MBq)	4 (iliq (1.8 to 7.5 GBq )	Lung =3 Liver =13

red marrow, the respective absorbed doses per unit administered activity were used to calculate the therapy activity. Mean tumor absorbed dose could also be estimated based on the mean geometric factor. Using EXCEL, largely automated, we are able to implement a patient specific maximum tolerated activity treatment-planning algorithm for Re-188 Lipiodol Therapy with basic instruments (Planar gamma Camera, well counter)<sup>18</sup>.

A biodistribution image is shown in Figure 1. There is mild localization of the radioconjugate in the lung, probably due to A-V shunting, in these large tumors. The kidneys were faintly visualized at 24, 48 and 72 hours, indicating minimal clearance via the kidneys. *In-vivo* stability appeared to be excellent.



Fig1. Biodistribution of Re-188 HDD Lipiodol after 24 hrs.

There were no significant change in WBC, ANC or Platelet count at 24 hours, one week, one month, or three months of follow-up in any of the patients treated. AFP levels generally decreased after treatment, though some are rising again at three-month follow-up. Most patients had CT scan evidence of reduced size or stable disease. It is important to note that most of these patients had advanced disease with large tumors. An important feature of this new therapy was that, patients who underwent this treatment had only a short stay in hospital and were able to resume their normal work in a week (good performance status).

From the spreadsheet data it has been observed can be seen that we have not always achieved treatment doses up to the maximum tolerated dose. This is due largely to constraints in labeling of Re-188 with HDD and subsequent extraction into Lipiodol. However, 3 patients have been treated with large doses of 165, 168 and 206 mCi Re-188 Lipiodol with no adverse effects. The bone-marrow radiation doses were negligible. The radiation doses to the lung were also small. The main limiting factor to higher dose Re-188 Lipiodol treatment appears to be the MTD to normal liver.

#### Adverse Effects

Most of the patients took the very well without any toxicity and were discharged in 48-72 hours. There was slight elevation ALT and AST at 24 hours in most patients. Bilirubin levels remained unchanged. Reported events were as follows: Mild nausea lasting 24 hours in two patients, mild right hypochondral pain in 6, low grade fever at 24 hours in 8 and vomiting on first day in 1 patient (Table-2).

#### Discussion

Iodine-131 Lipiodol has been used to treat inoperable HCC<sup>4</sup>. and in the adjuvant setting post-resection. Yttrium-90 microspheres delivered transarterially have also shown useful results for inoperable HCC<sup>5</sup>. Dancey, et al<sup>19</sup> reported a response rate of 20% and a median survival rate of 54 weeks in 22 patients using Yttrium-90 microspheres. Lau, et al<sup>20</sup> reported a median survival of 9.4 months (range 1.8 to 46.4 months) in 71 patients. The overall response rate in terms of changes in alpha-fetoprotein levels was 89% (partial response of 67% and complete response of 22%) among 46 patients with increased AFP levels. They also reported that there were 4 patients whose HCC became resectable following treatment with yttrium-90 microspheres of which 2 cases achieved complete remission. Ho et al<sup>21</sup> reported a 17% to 92% response rate as well as a case of complete remission of unresectable HCC using Iodine-131 Lipiodol. However, both these radioconjugates are rather expensive and have to be ordered specially from countries like Canada, France and Australia. Re-188 Lipiodol offers a convenient alternative for the developing countries. The W-188/Re-188 generator can be made available on site with a long useful shelf-life of 4-6 months, and is cost-effective. The average energy of Re-188 beta particles is similar to yttrium-90 and is high enough for tumouricidal effects. Post-treatment CT scans after 2 months showed good localization of lipiodol in the tumors. Most importantly, there are only few side effects from the Re-188 Lipiodol treatment, compared to the chemoembolisation.

<sup>iii</sup> The EXCEL Spreadsheet, specially designed for this study by our consultant Dr. Pat Zanzonica

of Memorial Sloan Kettering Cancer Center is easy to use. The calibration factor, counts per microcurie or counts/MBq is simply obtained using a standard source of Re-188 of known activity. Attenuation Correction is necessary for lung and liver, and these factors are easily obtained using a 10 mCi flood source acquisition with and without the patient. Proper ROI's must be drawn for lung, liver and tumor for accuracy. These attenuation correction factors are obtained on the day of admission, prior to treatment the following day.

The difficulty in the study has been obtained adequate activity of radiochemical<sup>^</sup> pure Re-188 Lipiodol, as there are occasional problems in concentrating the evaluate from the generator and in obtaining good labeling.

From the dosimetry data in the Spreadsheet we have observed that the gamma-camera dosimetry tends to "underestimate" the percentage of injected dose in the liver and tumor. From our imaging studies over 72 hours, there is good liver localization of the scout and treatment dose delivered transarterially, and mild lung uptake noted on the scan. There is good in-vivo stability of the Re-188 Lipiodol radioconjugate, as there is no thyroid or stomach visualization and only faint renal activity is seen. The lung uptake may be due to the nature of the Re-188 Lipiodol complex and/or arteriovenous shunting. The underestimation of liver and tumor dose may be inherent in using gamma-camera dosimetry for mixed high-energy gamma and beta-ray emitters.

This study has been designed to evaluate any possible side effects, of Re-188 Lipiodol treatment and normal organ dosimetry. We have not sought specially to ascertain HCC tumor dosimetry since this will be done under an on-going Phase-2 study.

#### Conclusion

Re-188 Lipiodol is an easily available radioconjugate for transarterial treatment of HCC. The right quantity of the radioconjugate can be delivered after "scout" dose dosimetry studies have been done, to spare normal liver and lung from excess radiation dose.

From the small number of patients studied, we have found this treatment to be safe with minimal

side effects, at a dose up to about 200 mCi of Re-188 Lipiodol. Although there appears to be some response to treatment, (and a few patients have had re-treatment) the efficacy of this new agent for the treatment of HCC has to confirm in a Phase-2 study.

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## The outcome of antithyroid drug treatment in patients with Graves' disease guided by TRH loading test

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### Abstract

In forty-three thyrotoxic patients a retrospective study was undertaken to investigate the relationship between various parameters and the remission of the Graves disease. TRH test was used an indicator of antithyroid drug treatment outcome. Various other parameters including clinical characteristics, serum thyroid hormones, TSH, thyroid autoantibodies and TSH receptor antibody titers were also determined. One and half years of the therapy most patients became clinical and biochemical euthyroid and had both of plasma total T3 and TSH normal response to the TRH test. We could not observe any significant differences on age, sex, age of onset and duration of the treatment, between the remission (A) and relapsed (B) groups. Twelve (27.9%) of 43 patients relapsed with in year and 31 (72.1) patients remained in remission more than one year. Both of "TSH and "T3 increments were significantly greater in a group A than group B ( $P < 0.01$  for "TSH,  $P < 0.01$  for T3 respectively). Among above biochemical parameters, Only plasma total T3 was significantly distinguished between those two group patients at one month before TRH loading test. It was  $106.1 \pm 15.5$  ng/dl for group A,  $124.3 \pm 15.3$  ng/dl for group B, ( $P$  value  $< 0.001$ ). Also the basal levels of plasma T3 were significantly lower in remission group ( $106.7 \pm 17.0$  ng/dl) in a group A,  $122.8 \pm 21.7$  ng/dl for group B,  $P$  value was 0.01). Other three female patients those did not include in this study still had absence of either T3 or TSH response to TRH test, even after long-term antithyroid drug treatment (range 18-36 months). In those patients' thyroglobulin binding inhibiting immunoglobulin (TB II) concentrations were significantly higher than either A or B group at one month before TRH test (range 20-45%). These findings similar to our (10) and others previous studies (8-13). It is concluded that plasma total T3 and TBII concentration are most useful practical indicator to evaluate the effect of the antithyroid drug treatment and both of plasma total T3 and TSH response to TRH test modulate by plasma total T3 concentration.

**Key words:** Thyroid releasing hormone (TRH), thyroid hormone, antithyroid drug

### Introduction

There are many studies were undertaken to find the parameters, which can predict the clinical course of a patient with Graves' disease after antithyroid drug withdrawal. These studies were performed with clinical parameters (Meng, et al 1982), specific tests for predicting recovery of the hypothalamic-thyroid axis<sup>110</sup>, various serum parameters such as serum thyroid hormone levels, TSH

receptor antibodies"<sup>19</sup>, and therapeutic regimens<sup>20,23</sup>. A regular TRH test during antithyroid drug treatment is useful in predicting the likelihood of remission<sup>8</sup>. The relapse of the Graves' disease significantly more often in patients with abnormal T3 response to TRH test comparing to patients with normal T3 response to TRH test at the end the treatment<sup>9</sup>. In one of the study previously done at our institute, we have studied free T3 and TSH

response to TRH in patients with patients with Graves' disease and have concluded that; the plasma free T3 levels may predict remission of Graves' disease after antithyroid drug treatment<sup>10</sup>.

In the present study, we report the plasma total T3 and TSH response to TRH test in-patients with Graves' disease and it's relationship to the remission. We have investigated retrospectively forty-three patients with Graves' disease were treated with antithyroid drug. The TRH test was used for monitoring outcome of antithyroid drug therapy.

## Materials and Methods

### Patients

Forty-three randomly selected patients, those who treated with antithyroid drugs and performed TRH test at end of the therapy were studied (11 men and 32 women, with mean age of  $42.7 \pm 12.6$  years). The patients divided into two groups according to outcome of treatment. A or remission group and B or relapsed group. The 31 patients (Group - A, 8 men and 23 women ) remained in remission for the observation period from 12-60 of months (mean $\pm$  SD,  $35.2 \pm 25.2$  months). Twelve of 43 patients with Graves disease (Group B, 3 men and 9 women ) relapsed within one year after stopping the drug treatment (mean $\pm$ SD,  $6.83 \pm 3.27$  of months) Table 1.

The diagnosis of relapse was considered in a patient with clinical manifestations of thyrotoxicosis in whom the plasma FT4 concentration was increased (over than 1.9 ng/dl) and plasma TSH concentration was suppressed (less than 0.32 U/ml) after stopping antithyroid drug treatment.

Table 1 Characteristics of the Patients with Graves' Disease.

Criteria	group A (Remission)	group B (Relapsed)	P value
Number of patients	31 (F 23. M 8)	12 (F9, M3)	
Age (yrs)	$42.3 \pm 13.4$	$40.2 \pm 10.9$	NS
Age of onset (yrs)	$37.4 \pm 12.4$	$37.9 \pm 11.1$	NS
Follow up period (mon)	$58.9 \pm 30.7$	$28.2 \pm 11.3$	0.001
Period of drug therapy (mon)	$22.6 \pm 15.3$	$21.1 \pm 10.6$	NS
Remission period (mon)	$36.5 \pm 26.3$	$7.0 \pm 2.8$	0.0004

F female. M male. " Mean + SD.

### Follow up

In all patients examined by one investigator and hormone and biochemical assay have done at central laboratory of our university hospital.

Patients were seen every 2 weeks until serum thyroid hormone levels became normal, which usually took 2-3 months, and they were followed every month thereafter, when stable euthyroid status established followed up at every 3 months.

### Protocol of treatment

Initial dose of methimazole was 30 mg/day, it was gradually reduced depending on serum concentrations of T-3, T-4, TSH and TBII. The patients who had an allergic reaction to methimazole the drug were replaced by propylthiouracil. The maintenance dose of methimazole and propylthiouracil were 5 and 50 mg/day, respectively.

### TRH test

When the patients became clinically and biochemically euthyroid, (normal range for TSH, 0.32-3.70 U/ml, FT-4, 0.7-1.9 ng/dl) while receiving the maintenance dose of antithyroid drugs, have performed TRH test for evaluate the recovery of the pituitary-thyroid axis. If TSH and T3 response blunted or subnormal, the therapy was continued, and the patients were reevaluated after another 3 months and if normal TSH and T3 responses were obtained, then withdrawn the drug therapy.

TRH tests were performed after an overnight fast by an iv injection of 500 mg synthetic TRH and blood samples were collected at before and 30, 60, 90, 120, 150 and 180 minutes after the test. An increment of TSH of 5-30 mU/ml, for T3 of 10-50ng/dl were considered normal, while less than 5mU/ml for TSH and 10 ng/dl for T3 indicated a blunted response.

### Statistical analysis

Grouped data were expressed as the mean $\pm$ SD, statistical significance was determined by Students t test.

## Results

There are no differences of mean age, onset of the disease and duration of the treatment between remission (A) and relapsed groups



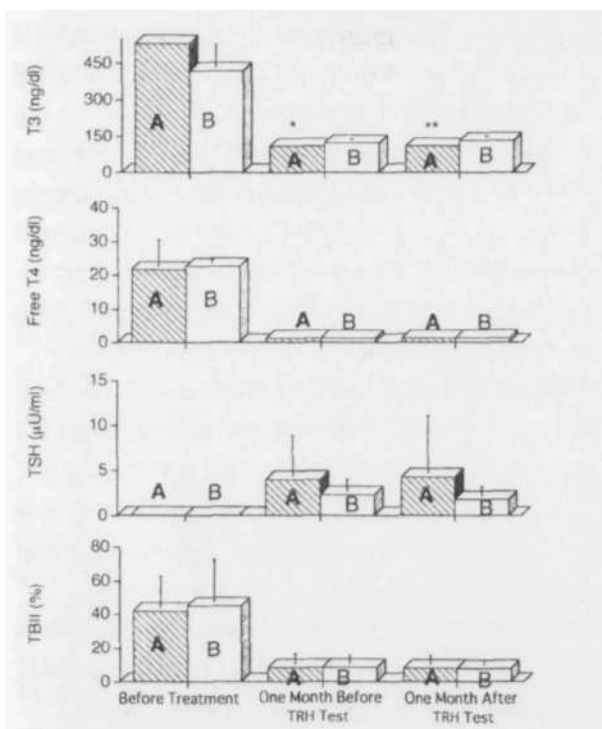


Fig.1. Serum T3, FT4, TSH and TBII levels in patients with Graves disease, before and after TRH test in groups A and B. Mean  $\pm$  S.D. values are shown. Differences between the two groups:\*, P<0.01; \*\*, P<0.001

after stopping the antithyroid drug treatment is shown in Fig. 1. Before antithyroid drug therapy, plasma T3, free T4 and TBII concentrations were high in all patients but not different among the two groups. At onset of the disease plasma total T3, T4 and TBII levels were 472.1 $\pm$ 235.9 ng/dl, 6.9  $\pm$ 4.5 ng/dl and 40.8 $\pm$ 22.7% in A group, 346.7 $\pm$ 63.2ng/dl, 6.2 $\pm$ 1 ng/dl and 45.3 $\pm$ 29.6% in B group respectively. At the time, one month before TRH test. Plasma T3 significantly low in remission (A) group, than relapsed (B) group (106.1 $\pm$ 15.5 ng/dl, 124.3 $\pm$  15.3 ng/dl, P<0.01). However, at the same time plasma free T4 and TBII, 1.1 $\pm$ 0.2 ng/dl, 8.3 $\pm$ 1.8% A group, 1.3 $\pm$ 0.3 ng/dl 11 $\pm$ 5.2% B group but not significant differences between the two groups. 3-6 months after antithyroid drug therapy, most patients became clinically euthyroid and thyroid hormone, TSH and TBII levels reached to normal range. Then the patients were took a maintenance dose of antithyroid drugs 5 mg of methimazole or 50mg of propylthiouracil during at least three months, then performed TRH test. The results of TRH tests are shown in Fig.2. The mean basal TSH value was 3.3 $\pm$ 2.6 mU/ml and the peak value of 28.3 $\pm$ 9.7 mU/ml was obtained at 30 min. after TRH administration in A group and B group it was 2.4 $\pm$ 1.8 mU/ml, 15.1 $\pm$ 9.3 mU/ml respectively. (Mean $\pm$ SD, P = NS for basal value, P<0.05 for at 30 min after TRH injection). The plasma total T3 gradually increased from the basal level of 106.7 $\pm$ 17 ng/dl to the peak value of 144.2 $\pm$ 24.6 ng/dl at 180 after TRH in A group and in B group it was 122.8 $\pm$ 21.7ng/dl, 143.9 $\pm$ 16.5ng/dl, respectively. (P<0.01 for basal levels and P= NS for at 180 minutes after TRH administration). Both of TSH and T3 increments (peak value - basal level) were significantly high in remission (A group) than relapsed (B) group. The mean increment of TSH was 25.7 $\pm$ 17.3, 12.5 $\pm$ 7.6 of mU/ml, P<0.01. and the mean increment were 37.7 $\pm$ 15.6, 24.0 $\pm$ 8.3 of ng/dl, P<0.01 (Fig. 3) There was no significant correlation among T3 and TSH increment after TRH administration. Both of T3 and TSH responses to TRH test has negatively correlated to plasma total T3 concentration (r=0.006 for " TSH, r=0.08 for " T3). There are no any correlation between the T3 and TSH responses to TRH test and plasma

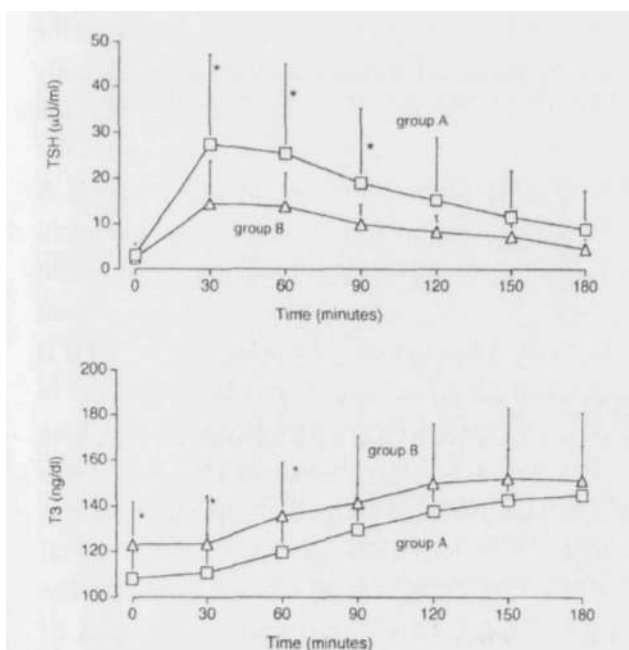


Fig.2. Plasma TSH (top) and T3 (bottom) responses to TRH in patients with Graves disease those who either remained in remission (A) or relapsed (B) group. Mean  $\pm$  S.D. values are shown. Differences between the two groups:\*, P<0.05.

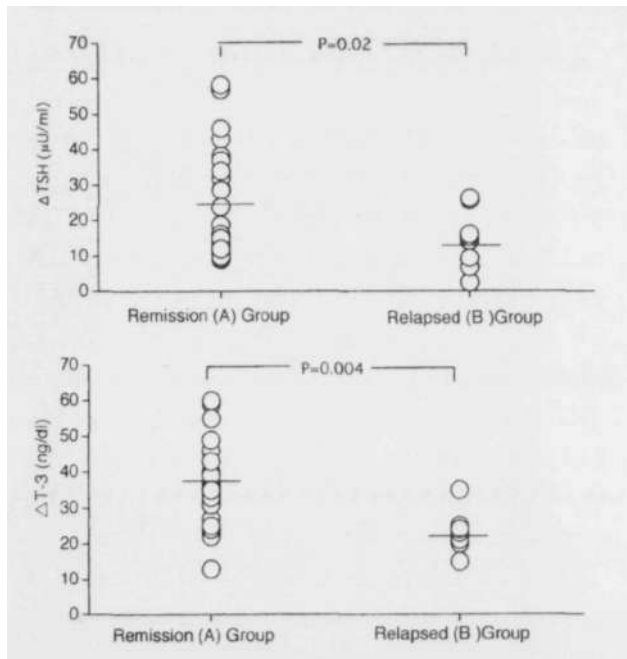


Fig.3. Plasma TSH (ATSH) and T3 (A T-3) levels above basal levels after TRH administration in patients with Graves disease in groups A and B. Horizontal lines indicate the mean values of A TSH and A T3.

free T4, TBII and thyroid receptor antibodies (AMA, ATA). Also in present study we could not observed any deference between remission and relapsed group, dose and duration of antithyroid drug treatment.

### Discussion

In the present study we examined the relationship basal, plasma total T3 levels and T3, TSH response to TRH test as an indicator of clinical course in patients with Graves' disease treated with antithyroid drug. Our previous study demonstrated that free T3 and TSH responses to TRH test were reliable parameters for evaluating the outcome of antithyroid drug treatment in patients with Graves' disease<sup>10</sup>. Also there many reports on the relationship between the remission of hyperthyroidism and various parameters and tests such as the T3 suppression test, TRH test, the serum triiodothyronine to thyroxine ratio<sup>7,10,8</sup>. Among those studies, several investigators evaluated plasma TSH response to the TRH test, and demonstrated that patients with a blunted TSH responses to TRH test at the termination of treatment, relapsed more often than those with a normal TSH response to TRH test<sup>4,8,10</sup>. In the present study we demonstrated that peak values

of plasma TSH appeared at 30 minutes after TRH administration, whereas plasma T3 levels reached their peak at 150-180 minute.

Increments in both plasma TSH (" TSH) and T3 (" T3 ) after TRH injection were significantly lower in patients with Graves' disease who relapsed than in patients who achieved remission (Fig. 3). Only one patient (69 years old women) who remained in remission had TSH hyperresponse (" TSH=221 mU/ml), but very small rise (" T3=7ng/dl) of T3 to TRH test and her plasma basal T3 level was 130ng/dl at before TRH administration. The plasma basal T3 levels were significantly low in remission group comparing to relapsed group ( $106.7 \pm 17$ ,  $122.8 \pm 21.7$   $P < 0.01$  respectively).

These findings similar to other investigators result (2-4), suggest that the TSH response to TRH test depend of the serum T3 concentration.

There are three female patients aged 27.5 + 14 of years (mean + SD), had long-term treatment of antithyroid drug (35.0 + 19.7 of months), but still have non response of both T3 and TSH to TRH test. In those patients, at one month before TRH test, plasma T3 (126 + 12.5 ng/dL) were a little higher but not significantly defer with A or B group, whereas TB II (18.2+8.7) concentration greater than threatened patients. The antimicrosomal (AMA) and the antithyroglobulin antibodies (ATA) at the end of antithyroid therapy did not show a statistically significant difference in the antibody titre between the patients of the relapse and those of the remission group<sup>9</sup>. This is also valid for our study. A positive TSA b index at the end of drug treatment was a useful indicator in predicting subsequent relapse of the disease". However, in our present study no statistical significant deference of TB II concentration between A and B group, but in patients treated with antithyroid drug during long term period, still no response to TRH test, it was higher than both of A and B group. However it is well known that TRH test one of the potential benefit test for evaluating pituitary-thyroid axis. The plasma total T3 concentration at the end of antithyroid drug treatment, gives useful information about the treatment effect and prognosis of TRH test. It way be, in patients with Graves' disease, when plasma total T3 reached lower limit of normal

range (less than 100 ng/dl) then would performed TRH test, it will be good result. From those findings we have concluded that, plasma total T3 and TBII concentration most useful practical guide of pituitary-thyroid axis recovery.

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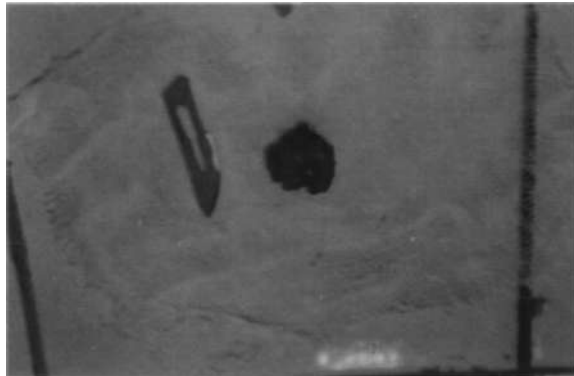
## Case Presentation

### Pancreatic ectopy in the stomach wall

O. Sergelen, B. Goosh  
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Health Sciences University of Mongolia,

A 45 year old woman presented with severe epigastric pain.

Previous history she had epigastric pain for a 5 years a on examination, she had a tenderness across the epigastrium. Exploration revealed a polyp 3 x 4 in the antrum of the major curve of the stomach.



only histologically . Histologic appearance is identical to pancreatic cell, cell of langergance and cell of pancreatic duct. Complication of the pancreatic ectopy is malignisation to the adenocarcinoma of stomach. Treatment is complete removal of the ectopy. Residual disease may lead to malignisation, and additional surgical procuders with added risk and complications.

Diagnosis of polyp of the stomach was made. At operation the polyp was completely removed. Polyp histology was pancreatic ectopy, completely excised. The patient recovered fully, and after a barium swallow demonstrating an intact mucosa, was discharged on the tenth postoperative day. The patient recovered from symptoms and is in good condition 2 years later., Pancreatic ectopy are very rare, estimated at 0.5 % and 13 % respectively, in Mongolia 0.013% Duodenum, small bowel and bil tract are the frequently affected areas diagnosed

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## Summaries of Ph.D theses in 2003

### Viral hepatitis C in women of reproductive age

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Viral hepatitis (HCV) is a common disease in the world as well as in Mongolia. Discovery of HCV in 1989 gives an opportunity to diagnose this disease. HCV infection takes place of 10.7-34.6% in whole population of Mongolia, 9.8% in children, 20.3% among cases of acute and 38.8-46.5% of chronic viral hepatitis and 59.1 -62.1 % in cases of hepatocellular carcinoma. To study the feature of clinical picture of HCV infection in Mongolian women of reproductive age and its natural history, to work out the methods of diagnosis and management. The study was carried out in 257 patients which divided into 173 patients with acute and 21 with chronic viral hepatitis C. The diagnosis was established by positive anti-HCV, anti-HCV-IgM and HCV-RNA by PCR, negative anti-HAV-IgM, HBsAg, anti-HBc-IgM, anti-HDV. The dominant age of patients with acute hepatitis C was 20-39 years (86.1%). Common ways of transmission were blood and blood products transfusion in 42.8%, birth delivery through Cesarean operation 17.3%, normal birth delivery 19% and other gynecological manipulations 15%. Incubation period lasted approximately for 46.7 days. In clinical picture mild form of hepatitis C occurred in 43.9%, moderate in 43.9%, and severe in 12.2%, as comparing to B viral hepatitis predominated mild form ( $p < 0.01$ ). In preicteric period dyspeptic syndrome proceeded in 85.5%, astenovegetative in 58.9%, lasting 4.9 days. During icteric period the predominant complaints were: loss of appetite 74.5%, discomfort in the epigastria part 59.5%, nausea 59.5%, epigastria pain 26.5%. 170 patients had typical form of disease and high level of bilirubin correlated with the severity of illness ( $p < 0.01$ ), in which the jaundice disappeared after 18.4 days. But the level of ALAT in acute viral hepatitis C did not correlate with the severity of the disease and in 52.6% fell to normal level. 50 patients with acute form of HCV infection were observed following up for 10 years, in which 24% did not have complaints, any clinical signs, negative HCV-RNA, 76% involved in chronic hepatitis. In our study were involved 36 women who were infected by acute viral hepatitis C during their pregnancy. 9 (33.3±9%) premature labours occurred in 27 labours. Premature labour and labour complications (rupture of amniotic fluid, powerless labour, uterine bleeding) in women with acute viral hepatitis C were 3-7 times more frequently than in healthy one. The pregnancy didn't influence on the disease progress. In comparison study 2b interferon therapy 21 women with chronic hepatitis C were treated for a long time, in which this therapy showed effectiveness in 42.8%, compared with men. Our study showed the beneficial effectiveness of right selection of the patients to the interferon therapy. Acute viral hepatitis C is commonly parenteral transmission. The incubation period of disease was short and the progress was severe ( $p < 0.01$ ) at the time of transfusion of blood and blood products, surgical manipulations, and these transmission associated. Clinical picture of acute viral hepatitis C has tendency to mild form, but the rate of chronicity is in a high level (76%). Interferon therapy in women with chronic hepatitis C is more effective than in men.

## Phytochemical investigations of *Oxytropis myriophylla* (Pall DC) and *Oxytropis pseudoglandulosa* (Gontsch ex Grub)

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*O. myriophylla* and *O. pseudoglandulosa* are the most popular components of many traditional prescriptions and named as "tag-sha" in Mongolian traditional medicine. The goal of this research was to isolate and elucidate the structures of the secondary metabolites of above two *Oxytropis* species and to carry out some pharmacological activity test of the extracts of these plants and develop the new preparation. Chemical constituents of the aerial part of *O. myriophylla* and *O. pseudoglandulosa* grown in Mongolia were studied. As a result of the investigation 19 compounds were isolated. 10 compounds were isolated from the aerial part of *O. myriophylla* and 5 of them were alkaloids, 3 were flavonoids and 2 of them were aromatic acids. N-trans-cinnamoyl-b-hydroxy-b-phenylethylamine was found to be novel natural compound and its structure has been elucidated. Absolute configuration of N-benzoyl-b-hydroxy-b-phenylethylamine was determined for the first time as 7S. The others were found for the first time from this species and alkaloid components of this species were studied for the first time too. 9 compounds were isolated from the aerial part of *O. pseudoglandulosa*. 3 of them are belonged to alkaloid and 6 of them are belonged to flavonoid. N-benzoyl-b-phenylethylamine, N-trans-cinnamoyl-b-hydroxy-b-phenylethylamine, pinocembrin, 7-hydroxyflavanone, 7-methoxyflavanone, 5-hydroxy-7methoxy-flavon, robinin were isolated from this plant for the first time. The technology of producing the preparation "Ortudent" from *O. myriophylla* worked out.

## A Study of disinfectant products in chlorinated drinking water in Ulaanbaatar

/ Chimedsuren

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Chlorination of drinking water is carried out to kill microbes that may exist in the water. It is known that this chlorination process could lead to the formation of "disinfectant by-products" (DBP's), some of which have been found to have carcinogenic properties. To date, trihalomethanes, haloacetic acids (HAAs), haloacetonitriles (HANs), and halo ketones (HKs) are some carcinogenic DBP's that are known to exist in the drinking water.

The chlorination of drinking water began in Mongolia in 1968, but to date the concentration of DBP's have not been surveyed. The aim of this study is to measure the concentration of THMs, HAAs, and HANs and to establish a relationship between precursors of some DBPs and the concentration of DBPs in the drinking water of Ulaanbaatar.

Three samples of water (raw, treated and tap water) was collected from stations A, B and V of the centralized system. Quality parameters of the drinking water were established using the universal EPA standards. The water concentrations of THMs, HAAs and HANs were measured using Gase chromatography, and calculated using Mathematical modeling.

It was found that the concentration of total organic compounds (TOC) in raw water samples were,  $1.32 \pm 2.01 \text{ mg/L}$  compared to  $0.68 \pm 1.23 \text{ mg/L}$  in treated water samples. It is thought that TOC's at this concentration level provide a favorable environment for the absorption of UV-254 and THM's and the formation of the DBP's in Mongolia's drinking water.

The concentrations of DBPs in Ulaanbaatar's drinking water were measured as follows; THMs =  $5.247 \pm 3.14$  mg/L, HAAs =  $1.288 \pm 1.181$  mg/L, HANs =  $0.50 \pm 0.133$  mg/L with the average content in tap water registering around  $4.173 \pm 2.43$  mg/L. The content of DBP's and inorganic compounds were found to be higher in the tap water at station V

The concentration level of DBP's estimated by Gase chromatographic analysis and Montgomery Watson was found to be similar. For this reason it is suggested that Montgomery Watson's model be utilized as it is simple and time and cost effective.

It is thought to be necessary to research and analyze the concentration levels of DBP's in Mongolia's drinking water as it will set a standard for water in Mongolia. It is also hoped that it will improve local monitoring and surveillance capabilities.

## **Some improvements of training content and staged training system of nursing education in Mongolia**

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The nursing care is an inherent part of health care system and international trend to its conception and tendency is undergoing substantial changes for last several years enabling to develop it as an independent nursing science. The existing nursing education content on each level can not meet current social needs despite the multi-level nursing education system used in Mongolia similarly as in other countries with developed nursing science. The existing nursing education program is still based on an old model of training of "feldshers" where nursing subject occupies less than 10 percent of the total subjects covered. Among the studied countries, the countries with developed nursing science use the credit system and have four levels nursing education system based on Diploma, Bachelor, Master and Doctor training. In order to improve quality of nursing care it is important to provide the Nursing Units at Health care institutions with professional management and trained nurses with Bachelor degree. The developed nursing education staged model is based on current economic capacity and social needs of the country and proposed as the best optimum version at present situation for nurses to improve their professional background at the working place.

## **Analysis of the root tantra (Four medical Tantras)**

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*School of Traditional Medicine, Health Sciences University of Mongolia*

The issue of reestablishment and development of research in Mongolian Traditional Medicine (MTM), has become serious question today. The MTM was introduced to Mongolia from India and Tibet many centuries ago. For everybody who is studying or working in the field of MTM, the most important point that must be studied is the first volume of the Four Tantras of Healing Science, entitled Root Tantra. The text of the Root Tantra is connected with other Tantric teachings by the system of 3 roots, 9 trunks, 47 branches, 224 leaves, 2 flowers and 3 seeds. Therefore, it is essential to analyse the profound content of the Root Tantra, and this is the main object of the research work. The research is aimed at: comparative study of the first volume Root Tantra of the series of the Four Tantra of the Healing Science; commentaries on that text; and clarifying profound and complicated understanding and terminologies of the text. In the research work we have studied the tradition of the Eastern Traditional Medicine, the complex properties of the buddist knowledge and it's elements were considered on time. The text of root



f the healthy body and the foundation of healing revealed that it is an origin to maintain body physiological balance. The real names and the colloquial names of natural materials used for medicines, methods of recognizing, selecting, and appropriate usage of them are all given in a systematic model. Traditional Medical training the "Drawing a tree" of "Root Tantra" introduced a complete and advanced training method of education. The research work signifies that Mongolian scholars have inherited the Eastern Traditional Medicine originated from Ayurveda, and have developed and enriched themselves the Traditional Medicine in a creative way.

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### **1. Editor in chief:** Tserenkhoo Lkhagvasuren, M.D., Ph.D., ScD

Graduated from Medical Institute of Mongolia, Faculty of Medicine in 1978. Trained as a physician in the Department of Anesthesiology and Intensive Care of Central Clinical Hospital, Ulaanbaatar. In 1989 appointed Head of Medical Information and Psychology Department of NMUM. The same year obtained PhD degree, NMUM. From 1991 to 1995 Director, Medical Education Unit of the NMUM. From 1995 to-date appointed as a president of the Medical Sciences University of Mongolia (now Health Sciences University of Mongolia). Currently serving as President of Consortium of Mongolian Universities & Colleges; Chairman of the Academic Council of the NMUM; President, Association of Mongolian Endocrinologists; Member of the Academic Council of Educational Research Institute, Mongolia; General Secretary of Mongolian Physiologist's Association; Chairman of Adolescence Future Center of Mongolia; Board member of the Asian Pacific Academic Consortium for Public Health. Published in the Annual Researcher's Conference, Asia Pacific Journal of Public Health and etc.

### **2. Editor:** Samdan Narantuya, BD., Ph.D., PDF

Graduated from Faculty of Photochemistry, Irkutsk State University, Russia in 1991. Obtained PhD degree in 1996 from Graduate School, Mongolian State University and Mongolian Academy of Sciences. 1996-1998 obtained several post doctoral fellowships from Aberystwith Institute of Grassland and Environmental Research, Wales, UK; Vienna University, Center of Pharmacy, Institute of Pharmacognosy, Vienna, Austria and Bonn University, Institute of Pharmacy, Bonn, Germany. She is also an expert of Tempus programme of European Commission. From 2002 to-date appointed Vice President of Research and Foreign Relations, Health Sciences University of Mongolia. Published in Chemistry of Natural Compounds; Studia biophysica, Scientia Pharmaceutica, Phytochemistry, Natural Medicines, Chem Pharm Bull, Journal of Natural Toxins, Journal of Chromatography, Helvetica Chimia Acta.

### **3. Associate Editor:** Bazar Amarsaikhan, DDS., Ph.D

Graduated from Faculty of Dentistry, Havana Medical University, Cuba in 1991. Trained as Instructor in the Department of Prosthodontics, School of Dentistry, NMUM. Obtained a PhD degree from Tokyo Medical and Dental University in 2002. From 1993 to 1997 worked as an assistant professor in the Department of Prosthodontics, School of Dentistry of NMUM. From 2002 to 2003 Senior Lecturer of Department of Prosthodontics and Chairman of International Relationships, School of Dentistry of NMUM and Chairman of Young Researchers Council of NMUM. From 2003 to-date appointed as Dean of Graduate Studies of HSUM. Served as president and or member of many national and international organizations such as Mongolian Dental Association; Japanese Prosthodontic Society, Japanese Association of Dental Research; International Association of Dental Research; Mongolian Chapter; Academy of Dentistry International. Published in the Journal of the Japanese Dental Association; Journal of Dental Research; and Journal of Medical and Dental Sciences.

### **4. Editorial Board:** Khasag Altaisaikhan, BD., Ph.D

Graduated from National Medical University of Mongolia, Faculty of Medicine in 1991. Having experience as a Lecturer at Microbiology Department, NMUM and an officer of the Medical Education Unit, NMUM. In 2002 obtained PhD degree in Shimane Medical University, Japan. From 2002 to 2003, Head of the Department of Endocrinology and Haematology, NMUM. From 2003 to present appointed

as Dean, School of Medicine, HSUM. Served as president or member of following national and international organizations such as Mongolian Diabetes Association; Mongolian Endocrine Association; Medical Young Researchers' Association of Mongolia; Endocrine Society; Japan Diabetes Association; International Diabetes Federation. Published in several biomedical research journals.

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Professor in general practice and department head of General Medical practice at Groningen University, The Netherlands, since 1990. A member of the editorial boards of the Dutch Scientific Journal for GPs; and the Dutch Medical Journal; of the advisory boards of the Ministry of Health: the Dunning Commission 'Choices in Health Care' and the Council for Health and Healthcare. Published in Family Medicine; BMJ, Eur Resp J, Neu-ro-e-pidemiology; Family Practice.

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Graduated from Yonsei University, College of Medicine in 1984. Postdoctoral Fellow and Senior Research Associate Julia McFarlane Diabetes Research Centre Faculty of Medicine, University of Calgary, Alberta, Canada; Research Associate at the Department of Physiology and Biophysics University of Southern California, School of Medicine Los Angeles, California, U.S.A. From 1998 to-date: Director of Central Research Laboratory, Health Sciences University of Mongolia; and Program Coordinator of Academic Exchange Program for Yonsei Medical Mission Center, Yonsei University Medical Center of Korea, in Mongolia. Published in Can J Microbiol Diabetes; Clin Inv Medicine; Can Med Ass J; Lancet; J of Diabetologia, J Gen. Virol, Pediatric Adolesc Endocrinol, Autoimmunity.

**7. Editorial Board:** Dagvasumberel Gonchigsuren M.D., Ph.D

Graduated from National Medical University of Mongolia, Faculty of Medicine in 1991. In 1994 obtained PhD degree from the Medical University of Mongolia. Currently, Head of the Department of Radiology, School of Medicine, Health Sciences University of Mongolia. Served as president and or member of many national and international organizations such as Mongolian Radiological Society and Radiological Society of North America. Published in World Journal of Nuclear Medicine; American Journal of Roentgenology; etc.

**8. Editorial Board:** Johann Jurenitsch, Ph.D

Graduated from Pharmacology at University of Vienna 1972. Obtained the PhD degree from University of Vienna, Austria. Worked as research assistant at the School of Pharmacognosy of the University of Vienna; presently working as researcher at Faculty of Natural Science of the University of Vienna; Professor of phytochemistry at the University of Saarlandes; Visiting Professor at the Organic Chemical School at the University of Ulm. Currently serving as vice president of University of Vienna. Published in Sci. Pharm; Planta medica; Chromatographia.J; Chromatogr.Sci. Pharm; Planta medica; Nutrition; Pharmazie Mikrochimica Acta; Phytochemistry; Tetrahedron; Ann. Chem.

**9. Editorial Board:** Karen Hein, M.D

Graduated from College of Physicians and Surgeons, Columbia University in 1970. Served as President, William T Grant Foundation. Obtained Postdoctoral Fellowships in Adolescent Medicine, Department of Pediatrics, Montefiore Medical Center; and WJ Health Policy Fellowship, Institute of Medicine, Washington, DC. Served on U.S. Senate Finance Committee Professional Staff; Executive Officer Institute of Medicine, National Academy of Sciences, Washington, DC; President, William T. Grant Foundation, NYC. Former Instructor, Assistant Professor, Associate Professor of Department of Pediatrics, Albert Einstein College of Medicine; Assistant Professor of Pediatrics, College of Physicians and Surgeons,

Columbia University, NYC; Associate Professor and currently Professor of Pediatrics; also Professor of Epidemiology and Population Health Albert Einstein College of Medicine, NYC. Member of the Society for Adolescent Medicine; Ambulatory Pediatric Association; American Academy of Pediatrics; American Federation for Clinical Research; American Medical Women's Association; American School Health Association; Section on Adolescent Health, American Academy of Pediatrics; New York Academy of Sciences; American Association for the Advancement of Science; Society for Pediatric Research; Society for Behavioral Pediatrics; Eastern Society for Pediatric Research; American Medical Association; Association of Reproductive Health Professionals; American Association of University Women; American Pediatric Society; The New York Academy of Medicine; Society of Medical Administrators. Published in *Acta Paed Scand Supplement*; *J Pediatr*; *Amer J Clin Nutr*; *Archives of Surgery*; *Clin Ped*; *Am J Dis Child*; *Pediatrics*; *American Psychologist* *JAMA*; *Ped Annals*.

**10. Editorial Board:** Nyamkhishig Sambuughin BD., Ph.D

Graduated from Irkutsk State University of Russian. Obtained PhD degree from Vavilov Institute of General Genetics at the Russian Academy of Sciences in 1992. From 2001 to-date appointed as Staff Scientist, Neurology Research, Barrow Neurological Institute, St. Joseph's Hospital and Medical Center, Phoenix, AZ. Obtained several postdoctoral fellowships from the Laboratory of Molecular Systematics Smithsonian Tropical Research Institute, Panama City, Panama; Clinical Neurogenetics Unit, Medical Neurology Branch, NINDS, NIH, Bethesda, MD; Research Associate, Neurology Research, Barrow Neurological Institute, St. Joseph's Hospital and Medical Center, Phoenix, AZ. Member of American Society of Human Genetics; Malignant Hyperthermia Association of the USA; Scientific Commission, Health Sciences University of Mongolia. Published in *Human Genetics*; *Am J Hum Genet*; *Acta Neuropathol*; *Neuromusc Disorders*; *Neurology Clin*, *Am J Hum Genet*; *Anesthesiology*; *JAMA*; *Clin Genet*; *Mol Biol Evol*; *J Neurol Sci*; *Ann Neurol*; *Genetics*; *Human Biol*; *Jpn J Human Genet*.

**11. Editorial Board:** Takayuki Masuda DDS., PhD

Graduated from Faculty of Dentistry, Tokyo Medical and Dental University in 1985. Obtained PhD degree in 1989 from the Tokyo Medical and Dental University. From 2001 to-date appointed as an assistant Professor, Fixed Prosthodontics, Department of Restorative Sciences, Division of Oral Health Sciences, Graduate School of Tokyo Medical and Dental University. Published in *J. Stomatol Soc*; *J. Jpn Prosthet Soc*; *J Jpn Stomatognathofunct*; *Int J Oral Maxillofac Implants*; *Dentistry in Japan*; *J Jpn Assc. Dent Edu*; *J. Med. Dent. Sci*; *Int. J. Prosthodont* .

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Graduated from National Medical University of Mongolia, Faculty of Medicine in 1982. In 1995 obtained PhD degree from the Medical University of Mongolia and 2002 Doctor of Science. Obtained several postdoctoral fellowships in Poland, Korean and Switzerland. Currently, Head of the Department of Surgery, School of Medicine, Health Sciences University of Mongolia. Served as member of many national and international organizations such Mongolian Society of Surgeons.

**13. Editorial Board:** G.Mikhail M.D

Graduated from Alexandria University School of Medicine, Alexandria, Egypt in 1955. Obtained several postdoctoral fellowships from Washington University School of Medicine, St. Louis, Missouri; Laboratory of Professor Diczfalusy Stockholm, Sweden; Laboratory of Professor J.Zander, Cologne, Germany. Worked as instructor and Assistant Professor in Obstetrics and Gynecology, Washington University School of Medicine, St. Louis, Missouri; Associate Professor in Obstetrics and Gynecology, Jefferson Medical College, Philadelphia, Pennsylvania; Visiting Professor in Obstetrics and Gynecology, The University of Texas Southwestern Medical School at Dallas, Texas; Associate Professor, Director of

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**14. Editorial Board:** Dr.Wiwat Rojanapithayakorn

Graduated from Mahidol University, Thailand in 1976. Obtained Master of Urban Public Health, Mahidol University and certified in Field Epidemiology, Thai Ministry of Public Health -World Health Organization & The United States Centers for Disease Control. Board certified in Preventive Medicine, Thai Medical Council. Obtained postdoctoral fellowship at Carleton University and University of Ottawa, Canada in public administration, micro- & macro-economics, statistics, public sector investment and pricing, planning and evaluation, health economics and organization behavior. Worked as clinician and Director of Yaha Crown Prince Hospital, Yala Province,Thailand; Chief Medical Officer Department of Communicable Disease Control, Ministry of Public Health of Thailand; Team Leader, UNAIDS Asia Pacific Intercountry Team, Bangkok; and Senior Technical Advisor, Asia/Pacific and the Middle East Division, Department of Country and Regional Support, UNAIDS, Geneva. Currently short-term consultant for, WHO Mongolia. Served as Chief Editor of the Communicable Disease Journal, Thailand and the Journal of the Thai Medical Society for the Study of Sexually Transmitted Diseases; founder and Chief Editor of the Journal of Health Science: Chief Editor of the Thailand's Health System Research Journal; Deputy Chief Editor of the Thai Medical Council Bulletin; Editor of the Communicable Disease Newsletter; founder and Editor of the AIDS Newsletter, Department of Communicable Disease Control; Editing Board of the Thai AIDS Journal; assistant Editor, Human Resources for Health Development Journal; editing Board of the Health Policy and Planning Journal, Thailand. Published more than 100 articles in the areas of communicable disease control and HIV/AIDS/STI, in the *Communicable Disease Journal*; *JAMA*; *Journal of Health Science*; *Lancet* etc.

**15. Editorial Board:** Dr. Andrew Singleton B.Sci., Ph.D

Received his B.Sc. (Hons) degree from the University of Sunderland, UK and Ph.D. from the University of Newcastle upon Tyne, UK where he studied genetic causes and contributors to dementia. Dr. Singleton performed his postdoctoral training at the Mayo Clinic in Jacksonville, Florida, studying the genetic basis of neurological diseases such as dystonia, ataxia, essential tremor, dysautonomia, stroke and Parkinson's disease. In 2001 he joined the NLA as an Investigator within the newly created Laboratory of Neurogenetics. Human geneticist whose research interests focus on the genetics of neurological disease.

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Example: Bold T, Gombo S, Aldarmaa S: Effect of a mixture of amino acid on gastric acid secretion. *Mon J Heal Sci* 2003; 1:23-25.

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Example: Zendmen A. History of the Mongolian Health Services. 2nd ed. Ulaanbaatar: Health Sciences University Press; 2003: 70-75.

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Example: Amarsaikhan B. Dental Emergencies. In: Tsolmon H (editor). *Manual of Dental Emergency*. 2nd edition. Ulaanbaatar, Health Sciences University of Mongolia Press; 1991:30-50.

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I, International Committee of Medical Journal Editors. Uniform requirements for manuscripts submitted to biomedical journals. *Br Med J* 1991;302:338-41.

2.41st World Medical Assembly. Declaration of Helsinki: recommendations guiding physicians in biomedical research, involving human subjects. *Bull Pan Am Health Organ* 1990; 24: 606-609.

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