Epidemiological Correlation Between Chromium Content in Gallstones and Cholesterol in Blood

AKIKO SHIGETA, M.D.*,
SUPACHAI RATANAMANEECHAT, M.D.**,
SONGPHOL SRISUKHO, M.D.***,
MIKIO TANAKA, Ph.D.*****
YUKICHI MORIYAMA, M.D.*,
SURAPOL SUWANAGOOL, M.D.**,
MASARU MIKI, M.D.****,

Abstract

The authors measured the chromium in gallstones and bile from patients in three areas (Kawasaki (a city adjacent to Tokyo) in Japan, Chiang Mai and Bangkok in Thailand) by means of neutron activation analysis. The chromium in three types of gallstones (cholesterol, pigment, and rare stones) and bile from patients living in Bangkok were evidently larger than those from patients living in Kawasaki and Chiang Mai. The high chromium intake by Bangkok patients continued from the start of gallstone formation until the time the stones were removed. The total-cholesterol, triglyceride, and hemoglobin A_{1C} levels in the blood from Bangkok residents with high chromium intake over a long period were clearly lower than those of Japanese and Chiang Mai residents. The authors showed that the high dietary intake of chromium over a long period may play a role in the lowering of total-cholesterol, triglyceride, and hemoglobin A_{1C} in blood.

Key word : Chromium Levels, Gallstones, Bile, Japanese, Thais, Total-Cholesterol, Triglyceride, Hemoglobin A_{1C}

SHIGETA A, MORIYAMA Y, RATANAMANEECHAT S, et al
J Med Assoc Thai 2002; 85: 183-194

* Center for Digestive Diseases, Second Hospital, Nippon Medical School, 1-396 Kosugi-cho, Nakahara-ku, Kawasaki 211-8533, Japan.
** Department of Preventive and Social Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand.
*** Department of Surgery, Faculty of Medicine, Chiang Mai University, Chiang Mai 50200, Thailand.
**** Yokohama Daijin Hospital, 1-21 Hie-cho, Minami-ku, Yokohama 231-0011, Japan.
***** Laboratory of Chemistry, Nippon Medical School, 2-297-2 Kosugi-cho, Nakahara-ku, Kawasaki 211-0063, Japan.

When the amounts of essential trace elements are more than or less than the essential levels for human life, disorders of the amounts cause many diseases[1-3]. To elucidate the correlation between the amounts of essential trace elements and the diseases, the amounts in the body and/or many organs have been studied extensively[1-3]. Chromium (Cr) level in a patient receiving long-term total parenteral nutrition (TPN) was clearly lower than normal levels, and clear diabetic symptoms were observed[4]. After infusion of Cr for 2 weeks, the patient's symptoms were alleviated[4]. Cr in plasma and urine from type 2 diabetics (Non-insulin dependence diabetic (NIDDM)) were about 33 per cent lower and about 100 per cent higher, respectively, than those from healthy people[5]. Type 2 diabetics receiving Cr picolinate for 4 months had lower plasma total-cholesterol (TC) and hemoglobin A_{1c} (HbA_{1C}) values[6]. Low–molecular-weight chromium (LMWCr) compounds isolated from the mammalian liver potentiate, the conversion of glucose into carbon dioxide and lipid[7], and activate phosphotyrosine phosphatase (PTP) activity in isolated adipocyte membranes[8]. Moreover, LMWCr increases tyrosin protein kinase activity of insulin-activated insulin receptor[9]. A similar synthesized chromium complex decreased TC, triglyceride (TG), and low-density-lipoprotein (LDL) cholesterol greatly in plasma of rats after 12 weeks' administration of the complex[10]. Feeding of a high-fat, low-Cr diet to rats induced insulin resistance, and this symptom was improved by administration of Cr[11]. Therefore, chromium is known to play an important role in the regulation of the glucose/insulin system and insulin sensitivity[12], but the daily intakes of 90 per cent of the American population and half that of developed nations were less than that based on an Estimated Safe and Adequate Daily Dietary Intake (ESADDI)[8,13,14]. Consequently, the authors thought that estimation of Cr intake over a long time and at the present time is very important.

In this study, the authors measured the amount of chromium (Cr) in the gallstones and bile of patients living in Japan (Kawasaki) and Thailand (Chiang Mai and Bangkok) by neutron activation analysis. The comparison of these areas provided information on the amounts of Cr intake from the diet and environment of patients during the period of gallstone formation and the present intake. The authors compared the amounts of total-cholesterol (TC), triglyceride (TG), and hemoglobin A_{1C} (HbA_{1C}) in blood and sera from people in a low- and high-Cr environment over a long period. This comparison showed that TC, TG, and HbA_{1C} levels in the high Cr area are clearly lower than those in low Cr areas.

MATERIAL AND METHOD

Classification of gallstones

The gallstones and bile were surgically obtained from patients suffering from cholelithiasis. The gallstones were classified as cholesterol, pigment or rare stones by morphology and infrared spectra analysis according to the criteria of the Japanese Society of Gastroenterology[15].

Gallstones and bile

The fifty-four Japanese gallstones and 40 bile samples used were obtained at the Center for Digestive Diseases, Second Hospital, Nippon Medical School, Kawasaki, Japan.

Seventy-four Thai (Chiang Mai) gallstones and 53 bile samples were obtained at the Department of Surgery, Maharaj Nakorn Chiang Mai Hospital, Chiang Mai, Thailand.

Thirty-nine Thai (Bangkok) gallstones and 47 bile samples were obtained at the Department of Surgery, Siriraj Hospital, Mahidol University, Bangkok, Thailand.

Blood and serum

Two hundred and fifteen Japanese blood and serum samples were obtained from healthy males and females on the occasion of medical examinations at the Health Administration Section in Internal Medicine, Second Hospital, Nippon Medical School, as shown in Table 1.

Sixty-five Chiang Mai blood and serum samples were obtained from healthy males and females on the occasion of medical examinations at Chiang Mai city, as shown in Table 1.

One hundred and eighteen Bangkok blood and serum samples were obtained from healthy males and females on the occasion of medical examinations at the Department of Preventive and Social Medicine, Siriraj Hospital, Mahidol University, as shown in Table 1.

Twenty-five tannery workers' serum samples were obtained at a tannery in the vicinity of Bangkok, as shown in Table 1.

Table 1. Age and sex of healthy Japanese and Thais (Chiang Mai and Bangkok), and tannery workers in a tannery in the vicinity of Bangkok whose blood and sera were analyzed for total-cholesterol, triglyceride, and hemoglobin A_{1C} (HbA_{1C}).

	Japanese		Thais					
			Chiang Mai		Bangkok		Tannery workers	
	Age		Age		Age		Age	
	Range	Mean ± SE	Range	Mean ± SE	Range	Mean ± SE	Range	Mean ± SE
Males	22-81	50 ± 1	29-73	47 ± 2	20-64	45 ± 2	18-72	38 ± 4
	(117)*		(33)		(59)		(16)	
Females	28-80	47 ± 1	31-69	50 ± 2	22-62	44 ± 1	18-50	32 ± 3
	(98)		(32)		(59)		(9)	
Both sexes	22-81	48 ± 1	29-73	48 ± 1	20-64	44 ± 1	18-72	36 ± 3
	(215)		(65)		(118)		(25)	

* The values in parenthesis are the number of samples analyzed.

Informed consent

After the authors explained the purpose of the gallstone and bile tests, and their clinical value for a patient and the purpose of the blood and serum tests, informed consent was obtained from the patients and healthy controls respectively.

Quantitative analysis of chromium

Measurement of chromium in gallstones and bile by neutron activation analysis

Each gallstone was ground to powder, weighed, and put into a polyethylene bag. Each bile sample was also weighed and put into a bag. Orchard Leaves (Standard Reference Material 1571, National Institute of Standards and Technology, MD, USA) was used as the standard for chromium analysis. The standard sample was weighed and put into a bag. All sample bags were irradiated for 24 h in a rotary specimen rack ($5X10^{11}$ n_{th} cm^{-2} s^{-1} at 100kW) in a TRIGA MARK II Reactor at the Institute for Atomic Energy, Rikkyo University, Yokosuka, Japan. After cooling for about 1 month, the activities of ^{51}Cr (half life: 27.7d) in samples were measured from 12,000 to 40,000 sec with a conventional 4,096 multichannel pulse high analyzer, and 80 cm^3 and 100 cm^3 pure Ge detector by using a characteristic gamma peak at 320 keV. The activities were corrected for decay to the end of the irradiation. To normalize the differences in the thermal neutron fluxes between the irradiation sites, and the counting conditions, the activities of standard samples were used. The authors determined the amount of chromium in gallstones and bile by calculating the ratio of the activities of chromium in the gallstones and bile to those of the standard samples. The detection limit under the measuring conditions was less than 1 ng.

Conditions for storage of serum

After two blood samples were taken from the same males or females, the serum in one sample was separated by centrifugation. The serum was stored at -5°C. The other sample was stored at 0°C. During transportation from Thailand to Japan by air, the serum and blood samples were stored in an ice box at -5°C and in an ice box at 0°C, respectively.

Quantitative analysis of total-cholesterol and triglyceride in serum

The amounts of total-cholesterol and triglyceride in the serum samples from the Japanese and Thai (Chiang Mai and Bangkok) males and females were determined by an enzymatic method at the Laboratory of Clinical Investigation, Second Hospital, Nippon Medical School.

Quantitative analysis of hemoglobin A_{1C} (HbA_{1C}) in blood

The percentage of HbA_{1C} in blood samples from the Japanese and Thais was determined with an immunoinhibition latex agglutination method by the same Laboratory.

Statistical analysis

Values were expressed as the mean ± SE. The authors performed the Kolmogorov-Smirnov two-sample test for the comparison of two samples. The Spjotvoll and Stoline test for multiple compa-

risons was used. The authors used STATISTICA (StatSoft, Inc., Tulsa, Okla.) for statistical analysis as ND (below the limit of detection) was zero. It was considered that P <0.08 indicated a significant difference, because the mean values for chromium content in each type of gallstone, and the mean triglyceride values have large standard deviations.

RESULTS

Chromium in cholesterol, pigment, and rare stones from Japanese and Thai patients

Significant differences in the mean values for chromium content were found between the values in cholesterol and pigment stones from patients living in Japan and Bangkok, and from Chiang Mai and Bangkok patients. A difference was found between the values in rare stones from the patients living in Chiang Mai and Bangkok, but the values in rare stones from Japanese and Bangkok patients had a large standard deviation, as shown in Table 2 and Fig. 1.

Chromium in bile from Japanese and Thai patients

Significant differences in the mean values for chromium content in bile were found between the values in Japanese and Bangkok patients, and in Chiang Mai and Bangkok patients, but the value for Japanese patients was similar to that for Chiang Mai patients, as shown in Table 3 and Fig. 2.

Amounts of total-cholesterol (TC) and triglyceride (TG) in sera, and hemoglobin A_{1C} (HbA_{1C}) in blood from Japanese and Thais

When the correlation coefficient between age and TC, age and TG, or age and HbA_{1C} was more than 0.4, statistical analysis for each correlation was not performed. The data with a coefficient of more than 0.4 were TC data from Japanese and Bangkok females, and TG from Japanese and Chiang Mai females, and HbA_{1C} from Japanese males.

Amount of total-cholesterol in sera

The mean TC value in sera from Bangkok males was significantly lower than those from Japanese and Chiang Mai males, as shown in Table 4 and Fig. 3. Moreover, the mean TC values for males and females working at a tannery in the vicinity of Bangkok were smaller than those for Bangkok males and females, with no significant difference, as shown in Table 7.

Amount of triglyceride in sera

The mean TG value in sera from Bangkok males was significantly lower than that from Chiang Mai males, as shown in Table 5 and Fig. 4.

The mean TG value in sera from Bangkok females was clearly lower than that from Chiang Mai females, with no significant difference, because the values from Chiang Mai and Bangkok females had high standard deviations.

Table 2. The chromium contents in gallstones, cholesterol, pigment, and rare stones from Japanese and Thai (Chiang Mai and Bangkok) patients (mean ± SE) ($\mu g\ g^{-1}$).

Residence	Gallstones (all types of stones)	Cholesterol stones	Pigment stones	Rare stones
Japan	2.26 ± 0.66 (n = 54)	0.85 ± 0.28 (n = 30)	4.76 ± 1.94 (n = 16)	2.50 ± 1.45 (n = 8)
		1	2	
Thailand				
Chiang Mai	2.70 ± 0.50 (n = 74)	2.86 ± 0.80 (n = 26)	2.60 ± 0.93 (n = 26)	2.63 ± 0.87 (n = 22)
		3	4	5
Bangkok	30.90 ± 9.48 (n = 39)	6.22 ± 1.68 (n = 11)	64.30 ± 20.55 (n = 16)	8.99 ± 3.07 (n = 12)

1: P <0.002, 2: P <0.0009, 3: P <0.07, 4: P <0.0006, 5: P <0.06.

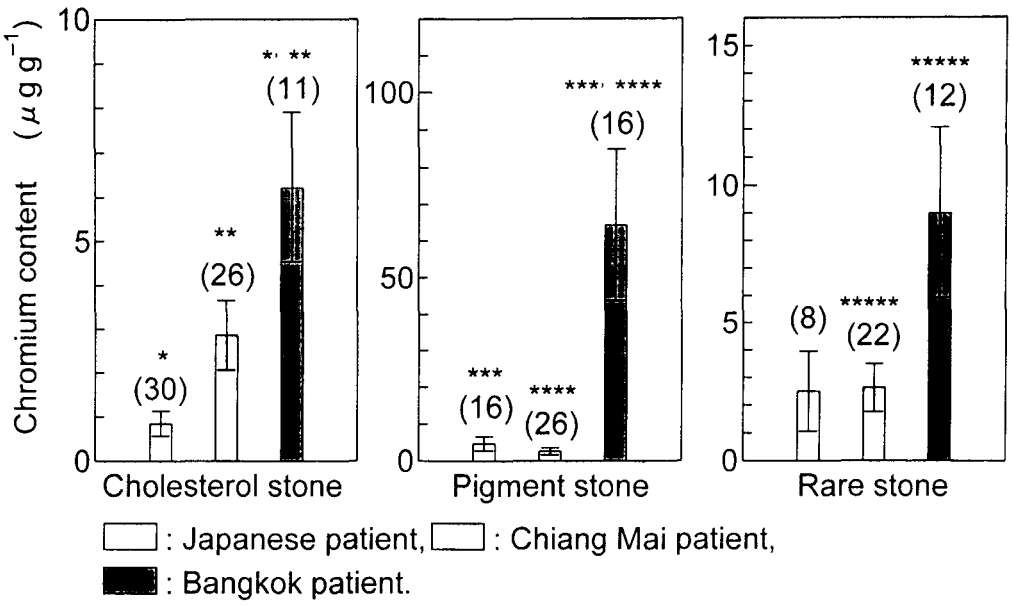

Fig. 1. **The chromium contents in cholesterol, pigment, and rare stones from Japanese and Thais (Chiang Mai and Bangkok) (mean ± SE). The values in parenthesis are the number of samples analyzed. *:P<0.002, **:P<0.07, ***:P<0.0009, ****:P<0.0006, *****:P<0.06.**

Table 3. The chromium contents in bile from Japanese and Thai (Chiang Mai and Bangkok) patients (mean ± SE) ($\mu g\ g^{-1}$).

Residence	Chromium contents	
Japan	2.71 ± 0.42 (n = 40)	1
Thailand		
Chiang Mai	2.03 ± 0.33 (n = 53)	2
Bangkok	4.99 ± 0.69 (n = 47)	

1: P <0.009, 2: P <0.0001.

Amount of hemoglobin A_{1C} in blood

The mean HbA_{1C} values in blood from Bangkok males and females were clearly lower than those from Chiang Mai males and females, with significant differences, as shown in Table 6. The mean HbA1C value in blood from Chiang Mai females was evidently greater than that from Japanese females with a significant difference. Moreover, the polygon of the HbA_{1C} value in blood from Japanese, Chiang Mai, and Bangkok females indicated that the peak position of the relative frequency for Bangkok females was placed on the lowest value on the polygon in contrast to those for Japanese and Chiang Mai females, as shown in Fig. 5. The relative frequencies of an HbA_{1C} value of less than 4.1 per cent from Japanese, Chiang Mai, and Bangkok females were 0.038, 0, and 0.136, respectively. Moreover, the frequencies of a value of more than 5.6 per cent from Japanese, Chiang Mai, and Bangkok females were 0.077, 0.375, and 0.068, respectively.

DISCUSSION

Serious chromium deficiency in females caused by long-term total parenteral nutrition (TPN), and obviously produced diabetic symptoms were observed[4]. After infusion of chromium for 2 weeks, the symptoms in the females were alleviated [4]. Feeding of a high-fat and low-Cr diet to rats induced insulin resistance, and the resistance was improved by a Cr diet[11]. Type 2 diabetes patients

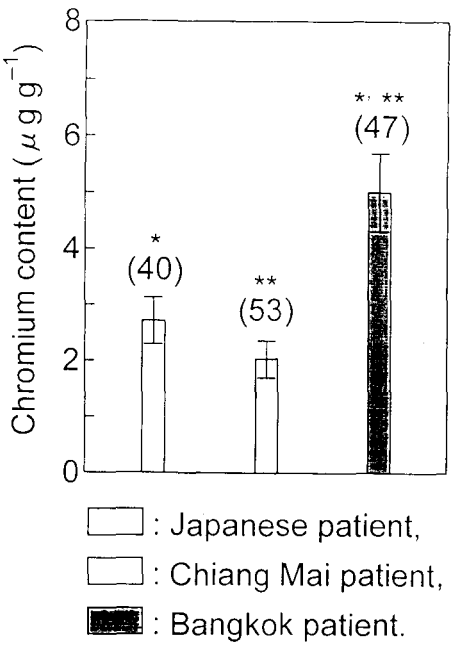

Fig. 2. The chromium contents in the bile from Japanese and Thais (Chiang Mai an Bangkok) (mean ± SE). The values in parenthesis are the number of samples analyzed. *:P<0.009, **:P<0.0001.

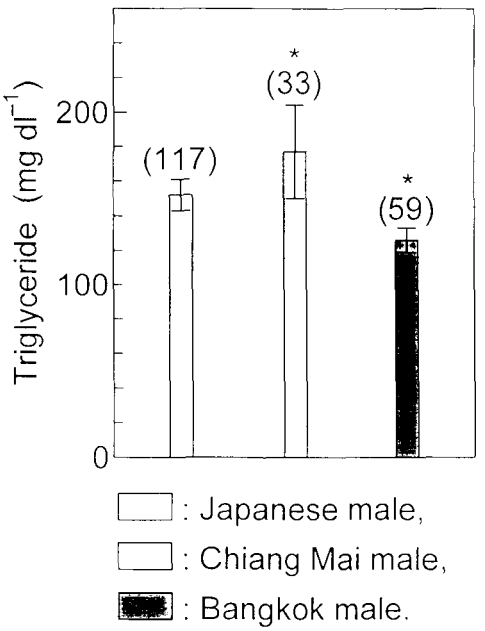

Fig. 3. The amount of total-cholesterol in sera from Japanese and Thai (Chiang Mai and Bangkok) males (mean ± SE). The values in parenthesis are the number of samples analyzed. *:P<0.022, **:P<0.0024.

Table 4. The amount of total-cholesterol in sera from Japanese and Thais (Chiang Mai and Bangkok) (mean ± SE) (mg dl^{-1}).

Residence	People	Male		Female
Japanese	203 ± 2 (n = 215)	204 ± 3 (n = 117)	1	203 ± 4 (n = 98)
Thais				
Chiang Mai	211 ± 5 (n = 65)	209 ± 6 (n = 33)	2	213 ± 8 (n = 32)
Bangkok	194 ± 4 (n = 118)	187 ± 5 (n = 59)		201 ± 6 (n = 59)

1: P <0.022, 2: P <0.024.

had mean levels of plasma Cr about 33 per cent lower and chromium values in urine almost 100 per cent higher than those found in healthy subjects[5]. The reduction in plasma chromium levels during the course of diabetes, although not correlated directly with insulin resistance, may contribute to defective insulin action[5]. In type 2 diabetes individuals receiving supplemental chromium (Cr) picolinate for

Table 5. The amount of triglyceride in sera from Japanese and Thais (Chiang Mai and Bangkok) (mean ± SE) (mg dl^{-1}).

Residence	People	Male	Female
Japanese	120 ± 6 (n = 215)	152 ± 9 (n = 117)	82 ± 5 (n = 98)
Thais			
Chiang Mai	153 ± 15 (n = 65)	177 ± 27 (n = 33)	127 ± 13 (n = 32)
Bangkok	114 ± 7 (n = 118)	126 ± 7 (n = 59)	103 ± 11 (n = 59)

1: P <0.08, 2: P <0.001.

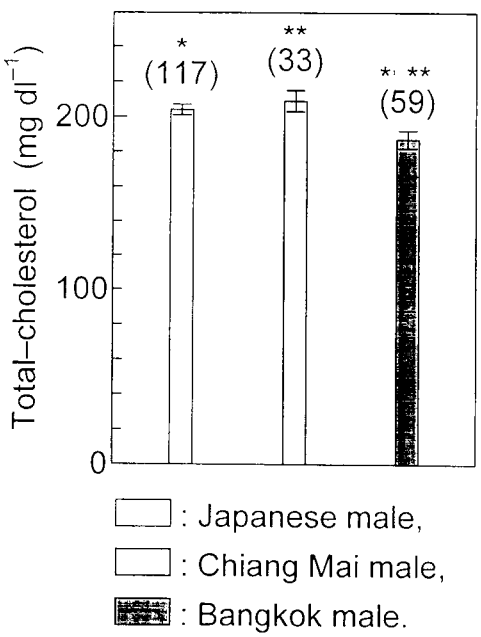

Fig. 4. The amount of triglyceride in sera from Japanese and Thai (Chiang Mai and Bangkok) males (mean ± SE) *:P<0.08.

4 months, plasma total-cholesterol (TC), hemoglobin A_{1C} (HbA_{1C}), and glucose values decreased[6]. A low-molecular-weight chromium (LMWCr) substance isolated from mammalian liver plays a role in carbohydrate and lipid metabolism as part of an insulin-signaling amplification mechanism[16]. A similar synthesized Cr compound decreased plasma TC and triglyceride (TG) in rats[10]. In Japan, 6.9 million people are thought to be diabetic, and this is 5.5 per cent of the population[17]. In the USA, 16 million people are estimated to have diabetes mellitus, which is 5.9 per cent of the population[18]. Type 2 diabetes accounts for about 90 to 95 per cent of all diagnosed cases of diabetes[18]. About 800,000 people per year are diagnosed with diabetes [18]. In many developing countries, such as Brazil, Iran, and Sudan, the dietary Cr intake is high, whereas in developed countries, such as Canada, Sweden, and USA, the intake is lower than 50 μ g/d which is in the lowest estimated safe and adequate daily dietary chromium intake range of 50-200 μ g/d (ESADDI) [13,14,19]. Therefore, we thought that studies of Cr intake over a long period and at the present time among different areas would be important. In fact, so far, no such studies have been reported. Over 40 per cent of orally dosed tris-(acetylacetonato) Cr (III) given to rats was absorbed from the gastrointestinal tract. As much as 45 per cent of the given dose was found in the bile[20]. After intraperitoneal injection of $K_2Cr_2O_7$ into mice, the greatest amount of LMWCr per mouse was observed in the liver (83 μ g), and the second greatest was in the kidneys (10 μ g). The amounts in other organs were 1 to 3 μ g[21]. It is known that gallstones are formed as a consequence of the coagulation of substances contained in bile. The authors therefore, thought that the amount of Cr in gallstones could reflect the Cr intake level over a prolonged period from the initial stage of gallstone formation until the time

Table 6. The amount of hemoglobin A1C in sera from Japanese and Thais (Chiang Mai and Bangkok) (mean ± SE) (%).

Residence	People	Male	Female
Japanese	4.9 ± 0.0 (n = 194)	4.8 ± 0.1 (n = 115)	4.9 ± 0.1 (n = 79)
Thais			
Chiang Mai	5.3 ± 0.1 (n = 65)	5.3 ± 0.1 (n = 33)	5.3 ± 0.1 (n = 32)
Bangkok	4.7 ± 0.1 (n = 118)	4.6 ± 0.1 (n = 59)	4.7 ± 0.1 (n = 59)

1: P <0.001, 2: P <0.001, 3: P <0.058, 4: P <0.0021.

Table 7. The amount of total-cholesterol in sera from healthy people and tannery workers living in Bangkok (mean ± SE) (mg dl^{-1}).

Sera		Male	Female
Healthy people	194 ± 4 (n = 118)	187 ± 5 (n = 59)	201 ± 6 (n = 59)
Tannery workers	181 ± 7 (n = 24)	179 ± 8 (n = 15)	186 ± 14 (n = 9)

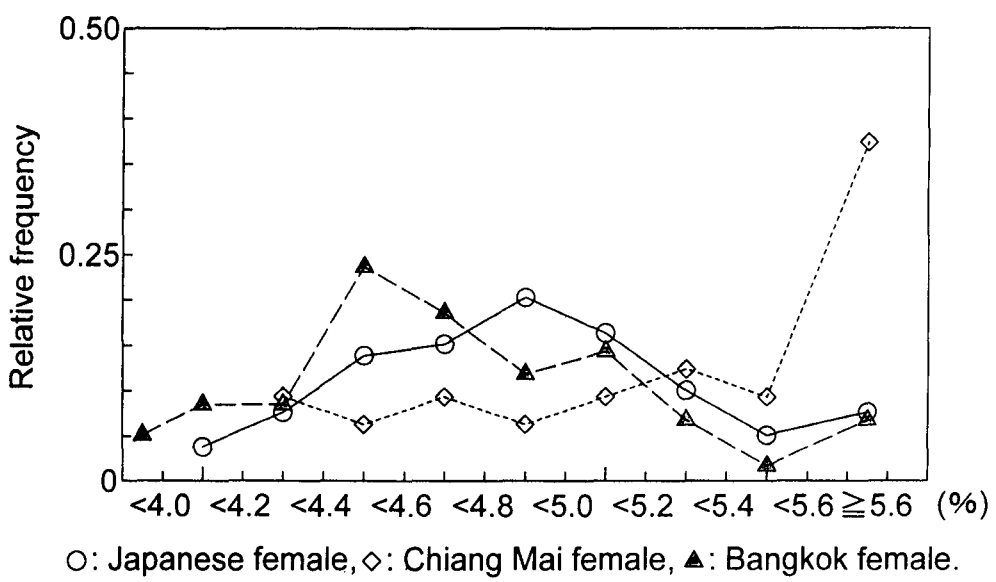

Fig. 5. The polygon of hemoglobin A_{1C} (HbA_{1C}) in sera from Japanese and Thai (Chiang Mai and Bangkok) females.

when the stones were removed. The authors investigated the Cr in gallstones and bile from patients living in Japan (Kawasaki) and Thailand (Chiang Mai and Bangkok) in an attempt to determine the chromium intakes over a long period for gallstone formation and at the time when the bile was collected, respectively. The relationship between the chromium in gallstones and bile, and TC, TG, and HbA_{1C} levels in people was also investigated.

Investigation as to whether the amount of Cr in gallstones from patients living in Japan, Chiang Mai, and Bangkok reflected a difference among the three areas in Cr intake was also undertaken. The mean values for Cr content in the three types of gallstones (cholesterol, pigment, and rare stones) from patients living in Bangkok were higher than in gallstones from patients living in Japan and Chiang Mai with significant differences. It was, therefore concluded that the amount of Cr in gallstones reflects Cr intake. Moreover, it was clear that the high level of Cr intake in the residents of the Bangkok district had continued for a long period until the gallstones were removed.

The authors then examined whether the amount of Cr in bile from patients living in the three areas reflected a difference in the Cr intake at the time when the bile was collected. The mean amounts of Cr in bile from Bangkok patients was greater than those in Japanese and Chiang Mai patients, with significant differences. This agreed with the authors' finding on Cr in gallstones. Gallstones are formed as a consequence of the coagulation of substances contained in bile. The noncholesterol sterols in gallstones are derived from the sterols in the diet, and their amounts can be altered by variations in dietary content[22]. The iodine in gallstones and bile reflects the iodine intake of residents[3]. The present results on chromium levels in gallstones and bile agree with those reports.

The comparison of the amount of chromium (Cr) in gallstones and bile from the three areas, therefore, showed that the Cr content reflects Cr intake. Moreover, this comparative study of the Cr in gallstones and bile from patients living in the three areas showed that the high Cr intake by residents living in Bangkok has continued from the initial stage of gallstone formation until now.

Analysis of the chemical composition of the Cr in gallstones or bile in this study was not performed.

The insulin secretion response to glucose in Cr deficient rats was twice as great as that in Cr supplemented rats for a compensation of peripheral insulin residence[23]. A positive correlation between post-prandial cellular cholesterol synthesis and insulin secretion was found in type 2 diabetics and non-diabetics with a high post-prandial insulin response[24]. Cholesterol synthesis is positively correlated with the residual insulin secretion in diabetics [25]. Moreover, insulin caused additional increases in 3-hydroxy-3-methylglutaryl coenzyme A (HMG CoA) reductase, the key enzyme in cholesterol synthesis in human mononuclear leucocytes[26]. Plasma TC decreased significantly with the supplement of Cr (19.2 μ mol/d) to type 2 diabetics for 4 months [6]. From an investigation of the amount of Cr in gallstones and bile, it was found that the Cr intake of Japanese and Chiang Mai people was lower than that of Bangkok people, and the low intake has continued over a long period from the initial stage of gallstone formation until now. The authors, therefore, compared the amounts of total-cholesterol (TC) in the three areas.

The amounts of TC in Japanese and Chiang Mai people were significantly larger than that in Bangkok. The amounts in Bangkok residents and tannery workers living in the vicinity of Bangkok were also compared, because the dietary intake of Cr for tannery workers was greater than that for the occupationally unexposed population[27]. The large intake of Cr may be caused by the absorption of leather dust, etc[27]. The amount of TC in Bangkok residents was greater than that in the tannery workers, with no significant difference. The authors indicated that the high dietary intake of chromium over a long period may play a role in the decrease in total-cholesterol in blood.

After rats were fed the low-chromium (Cr), high-fat diet for 16 weeks, they showed the presence of insulin resistance induced by the diet[11]. Moreover, a triglyceride (TG)-lowering effect in Cr adequate rats was observed in response to intravenous glucose administration compared with Cr deficient rats[11]. This effect is likely the result of two separate actions of insulin: one is activation of lipoprotein lipase, leading to an enhanced degradation of TG, and the other is concurrent suppression of lipolysis, resulting in a decreased supply of free fatty acids required for TG biosynthesis[11]. Cr is required for maintenance of the sensitivity of these

processes[11]. The high level of Cr intake by people in Bangkok in comparison with people in Japan and Chiang Mai has continued over a long period until the present. The amounts of TG in the three areas were, therefore, compared.

The amount of TG in Bangkok males was clearly smaller than in Chiang Mai and Japanese males. The authors showed that the high chromium condition of people in Bangkok over a long period may play a role in the triglyceride-lowering effect.

Cr translocates from the blood vessels to insulin-sensitive tissues (striated muscle and adipose tissue) along with insulin-dependent uptake of glucose[28]. This Cr uptake is clearly glucose-dependent in these tissues[28]. In the presence of insulin, LMWCr enhances glucose conversion to CO_2 (23-30% up) and lipid (30-40% up) in rat adipocytes [7]. Streptozotocin-induced diabetic and normal rats displayed a reduction in plasma glucose and plasma insulin levels after Cr administration for 4 weeks [29]. Cr administration improves both receptor affinity (insulin sensitivity) and postreceptor glucose transport (insulin responsiveness)[29]. After the supplement of Cr picolinate had been administered for type 2 diabetics over 2 months, HbA_{1C} values in diabetics decreased[6]. Because it was found that people in Bangkok have lived in a condition of high-Cr intake for a longer period than Japanese and Chiang Mai people, the authors compared the HbA_{1C} levels in these three areas.

The HbA_{1C} level of people in Bangkok was evidently lower than in Chiang Mai people. The authors showed that the high-chromium intake of the people of Bangkok over a long period may play a role in the improvement of the HbA_{1C} level.

The present results indicated that the high chromium intake in Bangkok residents has continued to the present. High-chromium intake may play a role in lowering total-cholesterol, triglyceride, and hemoglobin A_{1C}.

(Received for publication on November 18, 2001)

REFERENCES

1. Underwood EJ. Trace elements in human and animal nutrition. 4th ed. New York; Academic Press, 1977: 258-70.
2. Shils ME, Olson JA, Shike M (eds) Modern nutrition in health and disease. 8th ed. Pennsylvania; Lea & Febiger, 1994: 264-8.
3. Naito E, Pausawasdi A, Miki M, Tanaka M. Comparative studies on iodine levels in gallstones and bile of Japanese and Thais (Chiang Mai and Bangkok). J Med Assoc Thai 1999; 82: 374-82.
4. Jeejeebhoy KN, Greenberg G. Chromium deficiency, glucose intolerance, and neuropathy reversed by chromium supplementation, in a patient receiving long-term total parenteral nutrition. Am J Clin Nutr 1977; 30: 531-8.
5. Morris BW, Macneil S, Hardisty CA, Heller S, Burgin S, Gray TA. Chromium homeostasis in patients with type II (NIDDM) diabetes. J Trace Elements Med Biol 1999; 13: 57-61.
6. Anderson RA, Chen N, Bryden NA, Polansky MM, Chen N, Chi J, Feng J. Elevated intakes of supplemental chromium improve glucose and insulin variables in individuals with type 2 diabetes. Diabetes 1997; 46: 1786-91.
7. Yamamoto A, Wada O, Ono T. Isolation of a biological active low-molecular-mass chromium compound. Eur J Biochem 1987; 165: 627-31.
8. Davis CM, Sumrall KH, Vincent JB. A biologically active form of chromium may activate a membrane phosphotyrosine phosphatase (PTP). Biochemistry 1996; 35: 12963-9.
9. Davis CM, Vincent JB. Chromium oligopeptide activates insulin receptor tyrosine kinase activity. Biochemistry 1997; 36: 4382-5.
10. Sun Y, Mallya K, Ramirez J, Vincent JB. The biomimetic $[Cr_3O(O_2CCH_2CH_3)_6(H_2O)_3]^+$ decreases plasma cholesterol and triglycerides in rats: Towards chromium-containing therapeutics. J Biol Inorg Chem 1999; 4: 838-45.
11. Striffler JS, Polansky MM, Anderson RA. Dietary chromium decreases insulin residence in rats fed a high-fat, mineral-imbalanced diet. Metabolism 1998; 47: 396-400.
12. Anderson RA. Nutritional factors influencing the glucose/insulin system: Chromium. J Am Coll Nutr 1997; 16: 404-10.
13. Iyengar GV, Wolf WR, Tanner JT, Morris ER. Content of minor and trace elements, and organic nutrients in representative mixed total diet com-

posites from the USA. Sci Total Environ 2000; 256: 215-26.
14. Government of Canada. Chromium and its compounds. In: Canadian Environmental Protection Act. Priority Substances List Assessment Report. Ontario; Government of Canada, Minister of Supply and Services Canada, 1994.
15. The Japanese Society of Gastroenterology. New classification of gallstones in Japan (in Japanese). Nippon Shokakibyo Gakkai Zasshi (in Japanese) 1986; 83: 309-16.
16. Davis CM, Vincent JB. Chromium in carbohydrate and lipid metabolism. J Biol Inorg Chem 1997; 2: 675-9.
17. Ministry of Health and Welfare. Promoting measures against Life style-related diseases. In: Annual Report on Health and Welfare. Tokyo; Government of Japan, Ministry of Health, Labour, and Welfare, 1999.
18. The National Institute of Diabetes and Digestive and Kidney Diseases. Diabetes statistics. In: NIH Publication No. 99-3892. Maryland; National Institute of Health, 1999.
19. Kumpulainen JT. Chromium content of foods and diets. Biol Trace Elem Res 1992; 32: 9-18.
20. Anderson M, Riley D, Rotruck J. Chromium (III) tris-acetylacetonate: An absorbable, bioactive source of chromium. Fed Proc 1980; 39: 787.
21. Yamamoto A, Wada O, Ono T. Distribution and chromium-binding capacity of a low-molecular-weight, chromium-binding substance in mice. J Inorg Biochem 1984; 22: 91-102.
22. Tasaki T, Miki M, Tanaka M. Quantitative study of local distribution of noncholesterol sterols and cholesterol in gallstones. J Gastroenterol 1994; 29: 332-9.
23. Striffler JS, Polansky MM, Anderson RA. Overproduction of insulin in the chromium-deficient rat. Metabolism 1999; 48: 1063-8.
24. Griffin M, Frazer A, Johnson A, Collins P, Owens D, Tomkin GH. Cellular cholesterol synthesis-the relationship to post-prandial glucose and insulin following weight loss. Atherosclerosis 1998; 138: 313-8.
25. Feillet C, Monnier LH, Barjon JN, Perrin M, Descomps B, Crastes de Paulet A. Evidence for a short-term stimulatory effect of insulin on cholesterol synthesis in newly insulin-treated diabetic patients. Metabolism 1994; 43: 1233-40.
26. Krone W, Greten H. Evidence for post-transcriptional regulation by insulin of 3-hydroxy-3-methyglutaryl coenzyme A reductase and sterol synthesis in human mononuclear leucocytes. Diabetologia 1984; 26: 366-9.
27. Stupar J, Vrtove M, Kocijancic A, Gantar A. Chromium status of tannery workers in relation to metabolic disorders. J Appl Toxicol 1999; 19: 437-46.
28. Morris BW, Gray TA, Macneil S. Glucose-dependent uptake of chromium in human and rat insulin-sensitive tissues. Clin Sci 1993; 84: 477-82.
29. Yoshimoto S, Sakamoto K, Wakabayashi T, Masui H. Effect of chromium administration on glucose tolerance in stroke-prone spontaneously hypertensive rats with streptozotocin-induced diabetes. Metabolism 1992; 41: 636-42.

การศึกษาความสัมพันธ์ทางระบาดวิทยาระหว่างระดับปริมาณโครเมี่ยมของก้อนนิ่วและไขมันในเลือด

Akiko Shigeta, M.D., Yukichi Moriyama, M.D.*,*
*ศุภชัย รัตนมณีฉัตร, พ.บ.**, สุรพล สุวรรณกูล, พ.บ.**,*
*ทรงพล ศรีสุข, พ.บ.***, Masaru Miki, M.D.****, Mikio Tanaka, Ph.D.******

คณะผู้วิจัยได้ทำการศึกษาระดับโครเมี่ยมของก้อนนิ่วและน้ำดีจากผู้ป่วยใน 3 เขตพื้นที่ได้แก่มลฑลคาวาซากิ (ใกล้กรุงโตเกียว) ประเทศญี่ปุ่น, เชียงใหม่และกรุงเทพ ฯ โดยวิธี neutron activation analysis ค่าเฉลี่ยระดับโครเมี่ยมในก้อนนิ่ว 3 ชนิด (cholesterol, pigment, rare stone) และน้ำดีจากผู้ป่วยในกรุงเทพ ฯ มีค่าสูงกว่ากลุ่มผู้ป่วยมลฑลคาวาซากิและเชียงใหม่ จากการศึกษานี้พบว่า ผู้ป่วยที่มีนิ่วในถุงน้ำดี ซึ่งมีส่วนประกอบของโครเมี่ยมสูงที่อยู่ในกรุงเทพ ฯ เป็นผู้ได้รับโครเมี่ยมสูงมาตั้งแต่นิ่วก่อตัวขึ้นในถุงน้ำดี จนกระทั่งได้รับการผ่าตัดเอานิ่วออก นอกจากนี้ยังพบระดับ cholesterol, triglyceride และ hemoglubin A_{1C} ในเลือด ประชากรกรุงเทพ ฯ ผู้ซึ่งได้รับสารโครเมี่ยมจำนวนมากเข้าร่างกายเป็นเวลานาน จะมีค่าต่ำกว่าของประชากรญี่ปุ่นและเชียงใหม่

คณะผู้ทำการศึกษาแสดงให้เห็นว่าการได้รับโครเมี่ยมจากสารอาหารมาเป็นเวลานานมีบทบาทสำคัญในการทำให้ระดับของ cholesterol, triglyceride และ hemoglubin A_{1C} ในเลือดต่ำได้

คำสำคัญ : ความสัมพันธ์ทางระบาดวิทยา, ระดับปริมาณโครเมี่ยมของก้อนนิ่ว, ระดับปริมาณไขมันในเลือด

Akiko Shigeta, Yukichi Moriyama, ศุภชัย รัตนมณีฉัตร, และคณะ
จดหมายเหตุทางแพทย์ ฯ 2545; 85: 183-194

* Center for Digestive Diseases, Second Hospital, Nippon Medical School, 1-396 Kosugi-cho, Nakahara-ku, Kawasaki 211-8533, Japan.

** ภาควิชาเวชศาสตร์ป้องกันและสังคม, คณะแพทยศาสตร์ศิริราชพยาบาล, มหาวิทยาลัยมหิดล, กรุงเทพ ฯ 10700

*** ภาควิชาศัลยศาสตร์, คณะแพทยศาสตร์ มหาวิทยาลัยเชียงใหม่, เชียงใหม่ 50200

**** Yokohama Daijin Hospital, 1-21 Hie-cho, Minami-ku, Yokohama 231-0011, Japan.

***** Laboratory of Chemistry, Nippon Medical School, 2-297-2 Kosugi-cho, Nakahara-ku, Kawasaki 211-0063, Japan.