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Determination of Metal Content in Three Types of Human Gallstone

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In general, human gallstones formed in the bile cyst and/or bile duct are classified into three major groups such as cholesterol stone, pigment stone and rare stone. Each group can further be divided into subgroups: cholesterol stones into pure cholesterol stone, combination stone and mixed stone; pigment stones into calcium bilirubinate stone and black stone; and rare stones into calcium carbonate stone, calcium fatty acid stone, other combination stone and miscellaneous (Matsushiro and Suzuki 1984).

It is well known that metals are minor components in the vital body and they play very important roles for the biological functions. There are evidence that support some relationship between diseases and metals, being especially in cadmium and lead (Baum and Worthen 1967; Steassen et al. 1984). Many investigators reported concerning the components of the stone (Elliot 1973). Metal content in human renal calculi was reported previously (Yamamoto et al. 1987), but no paper have dealt with metal contents in relation to formation mechanism of gallstone.

In this study, we have determined the eight metal contents, i.e. calcium, magnesium, manganese, iron, copper, zinc, cadmium and lead, in gallstone. We focused on the metal contents in human gallstones and discussed the differences of metal contents in the various components, and the age and sex differences in the metal contents of the gallstones. We also discussed the relationship between metals and formation mechanism of gallstone as well as the environmental contamination.

MATERIALS AND METHODS

Standard solution of metals, perchloric acid and nitric acid were obtained from Wako Pure Chemicals Co. Ltd. Osaka, Japan for heavy metal analysis. And all other chemicals in extra pure grade were also purchased from the same source. Deionized and distilled water was used through the experiments. Ninety seven gallstones were collected from patients who were operated in Department of Surgery, Tohoku University School of Medicine. Stones

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were optically classified into three types of cholesterol stone and two types of pigment stone by the method of Matsushiro and Suzuki (1984). These were twelve pure cholesterol stones, seven combination stones, twenty three mixed stones, thirty eight calcium bilirubinate stones and seventeen black stones. The age range of patients were from twelve to eighty seven years old. Then, they were divided into three groups according to ages (12-39, 40-59, 60-). Sex composition was 35 for men and 62 for women.

The preparation of the samples was carried out by the wet digestion method reported previously (Yamamoto et al. 1987). A Japan Jarrel Ash atomic absorption spectrophotometer AA-8500 with a flameless atomizer FLA-100 and a concentration read out system MC-100, and a Hitachi Model 308 atomic absorption spectrophotometer were used for the determination.

Metal contents were compared with the data which we previously reported (Suzuki et al. 1975; Yamamoto et al. 1981, 1982a, 1982b, 1987) and other investigators reported about biological samples (Butt et al. 1964; Schroeder and Tipton 1968).

RESULTS AND DISCUSSION

Eight metal contents of gallstones were determined in ninety seven samples (Fig. 1). Contents of essential metals such as calcium, magnesium, manganese, iron and zinc were relatively higher than those of poisonous ones (cadmium and lead). Actually the order of metal content was calcium > magnesium > copper > iron > manganese > zinc > lead > cadmium (Table 1).

Metal contents of pigment stone were relatively higher than those in cholesterol stones. The order of metal contents of the gallstones was black stone > calcium bilirubinate stone > cholesterol stone (combination stone ≒ pure cholesterol stone ≒ mixed stone). All gallstones contained much calcium, magnesium and copper (Table 2).

Significant age difference was not observed in the content of all metals. In general, however, there was a tendency that 40-59 years old group had more metal contents than other groups (Table 3). Sex difference in the metal contents was not observed (Table 4).

Most of trace metals are essential elements for living cells and the contents are less than one part per million or less than iron content in living organism. In this study, manganese, copper and zinc are categorized as the essential elements. As compared with plasma or other biological samples, the metal contents were higher in gallstones. Manganese and copper contents in the gallstone were higher than those in urinary calculi (Yamamoto et al. 1982a; Yamamoto et al. 1987) and the level of all metals determined in the present study were almost the same as those in the previous work using other gallstone samples (Suzuki et al.

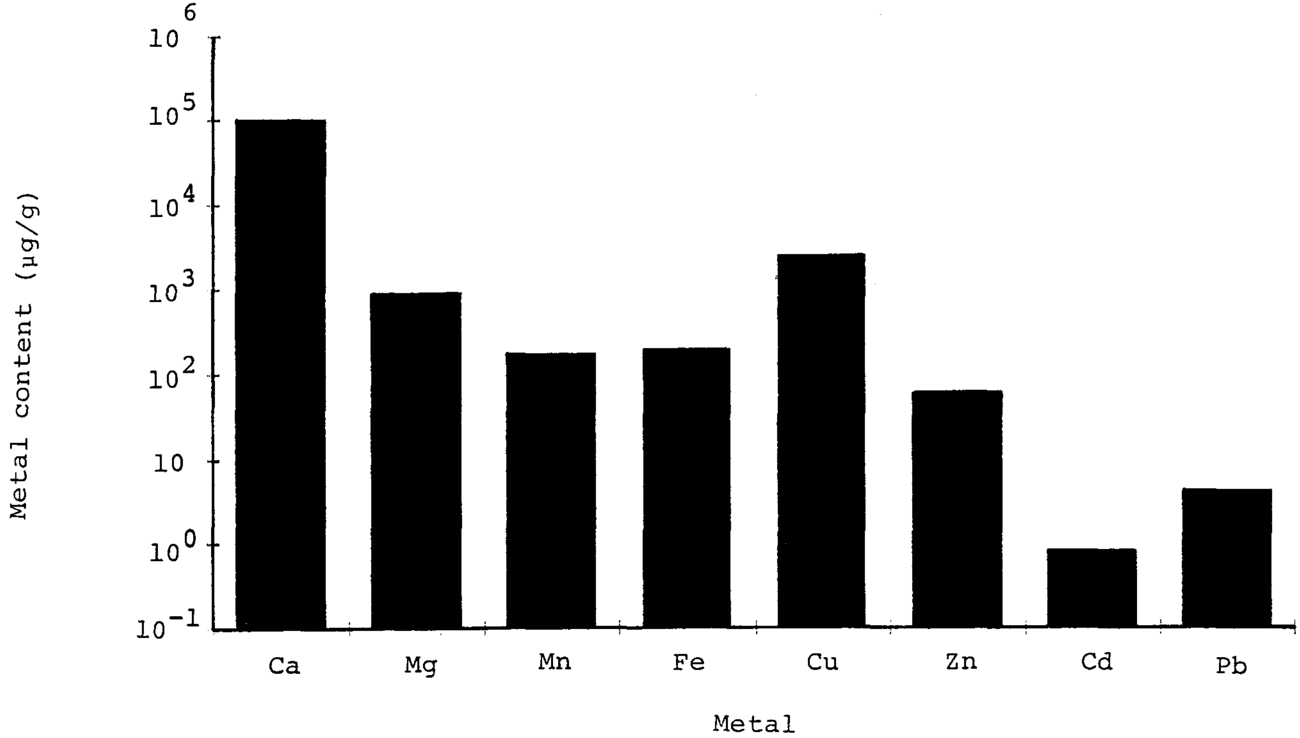

Figure 1. Metal content of human gallstone

Table 1 Metal contents in three different components of human gallstones

	Metal contents (mean ± S.E.)							
	Ca(mg/g)	Mg(μg/g)	Mn(μg/g)	Fe(μg/g)	Cu(μg/g)	Zn(μg/g)	Cd(ng/g)	Pb(ng/g)
Cholesterol	38.27	238.7	30.04	17.60	47.21	1.64	8.51	301.1
(N=42)	± 10.2	± 95.1	± 9.90	± 7.85	± 10.6	± 1.15	± 2.54	± 127
Incidence (%)	100	92.9	71.4	31.0	83.3	4.8	31.0	54.8
Ca bilirubinate	130.8	525.5	123.7	122.2	1978	72.96	206.5	2392
(N=38)	± 9.76	± 51.7	± 25.2	± 28.0	± 6875	± 22.6	± 50.5	± 405
Incidence (%)	100	100	92.1	100	100	97.4	100	100
Black	209.3	33.25	663.8	778.5	9613	164.3	4253	17490
(N=17)	± 46.11	± 625	± 189	± 205	± 3330	± 29.6	± 1620	± 468
Incidence (%)	100	100	100	100	100	100	100	100

Table 2 Metal contents of cholesterol stones

	Metal contents (mean ± S.E.)							
	Ca(mg/g)	Mg(μg/g)	Mn(μg/g)	Fe(μg/g)	Cu(μg/g)	Zn(μg/g)	Cd(ng/g)	Pb(ng/g)
Pure cholesterol	39.74	370.5	44.73	18.41	23.38	3.19	12.46	443.5
(N=12)	± 16.5	± 284	± 27.9	± 9.93	± 13.3	± 3.19	± 6.69	± 359
Incidence (%)	100	66.7	66.7	25.0	66.7	8.3	33.3	50.0
Combination	48.79	424.2	67.19	10.03	57.08	4.34	16.32	579.1
(N=7)	± 24.4	± 280	± 30.57	± 6.07	± 23.5	± 4.43	± 6.82	± 456
Incidence (%)	100	100	85.7	42.9	100	16.7	57.1	57.1
Mixed	34.29	113.5	11.07	19.49	56.64	ND	4.08	142.2
(N=23)	± 15.2	± 40.8	± 3.59	± 13.4	± 16.54		± 2.09	± 33.8
Incidence (%)	100	95.6	69.6	30.4	91.3	0	21.7	56.5

ND: not detected

Table 3 Comparison of metal contents of human gallstones in different ages

	Metal contents (mean ± S.E.)							
	Ca(mg/g)	Mg(μg/g)	Mn(μg/g)	Fe(μg/g)	Cu(μg/g)	Zn(μg/g)	Cd(ng/g)	Pb(ng/g)
Cholesterol								
0-39	51.68	81.18	8.43	ND	15.91	ND	ND	67.33
(N=8)	± 24.3	± 29.5	± 3.36		± 7.59			± 35.2
40-59	32.38	378.2	48.33	14.11	55.68	3.62	12.69	520.5
(N=19)	± 12.2	± 202	± 20.2	± 5.23	± 13.8	± 2.51	± 4.91	± 273
60-	38.56	146.0	18.40	31.41	53.17	ND	7.76	147.9
(N=15)	± 21.0	± 62.5	± 8.79	± 20.8	± 23.6		± 3.07	± 45.0
Ca bilirubinate								
0-39	116.4	586.0	34.96	73.52	6630	29.63	79.96	2368
(N=3)	± 29.8	± 311	± 17.6	± 24.8	± 6160	± 16.0	± 56.7	± 886
40-59	125.1	601.2	165.3	140.9	2700	95.78	233.4	2462
(N=12)	± 128	± 94.1	± 61.2	± 63.5	± 1530	± 63.9	± 128	± 859
60-	134.9	478.1	113.5	118.9	996.1	66.71	194.6	2359
(N=23)	± 14.5	± 61.0	± 26.2	± 33.0	± 264	± 18.0	± 51.7	± 503
Black								
40-59	236.5	3242	604.2	747.6	12470	156.7	3863	15529
(N=9)	± 80.2	± 1060	± 237	± 257	± 5800	± 30.2	± 1680	± 4700
60-	178.6	3419	730.8	813.2	6400	172.8	4693	20580
(N=8)	± 42.5	± 164	± 41.2	± 46.3	± 718	± 11.8	± 322	± 1060

ND: not detected

Table 4 Comparison of metal contents of human gallstones in the male and female

	Metal contents (mean ± S.E.)							
	Ca (mg/g)	Mg(μg/g)	Mn(μg/g)	Fe(μg/g)	Cu(μg/g)	Zn(μg/g)	Cd(ng/g)	Pb(ng/g)
Cholesterol								
Male	49.76	272.9	26.78	31.98	33.05	2.34	4782	310.3
(N=13)	± 25.1	± 167	± 17.0	± 23.6	± 12.6	± 2.34	± 2990	± 251
Female	33.11	223.4	31.50	11.16	53.55	1.32	10.18	297.0
(N=29)	± 9.76	± 118	± 12.3	± 4.37	± 14.3	± 1.32	± 3.42	± 148
Ca Bilirubinate								
Male	127.7	547.5	87.24	90.26	1936	44.38	107.6	2085
(N=15)	± 6.93	± 71.0	± 23.1	± 23.3	± 1220	± 10.6	± 21.8	± 619
Female	132.0	511.2	147.5	143.1	2007	91.60	256.7	2592
(N=23)	± 15.6	± 72.9	± 38.4	± 43.6	± 834	± 36.5	± 80.5	± 540
Black								
Male	121.9	3072	305.3	742.9	13430	156.4	5144	25450
(N=7)	± 35.4	± 794	± 70.6	± 309	± 6920	± 35.3	± 2300	± 9700
Female	270.4	3502	914.7	803.3	6939	169.8	3631	12620
(N=10)	± 69.5	± 936	± 298	± 287	± 3030	± 45.4	± 2330	± 4340

1975; Yamamoto et al. 1982b). Manganese and copper were condenced in gallstones, especially in pigment stones (Butt et al. 1964). So poisonous metals such as cadmium and lead might also be condenced in gallstones.

It is not the case of gallstones but Mayer and Angino (1977) reported that alminium, copper, tin and zinc prevented the formation of calcium phosphate stone, and Eusebio and Elliot (1967) reported that contaminant metals such as cadmium, mercury, manganese and nickel facilitate the formation of calcium oxalate stone. So manganese and cadmium may facilitate the formation of gallstones, especially pigment stones which contain much inorganic components. The results obtained in the present study indicate that metals, especially contaminants, can play some role in the formation mechanism of gallstones. Moreover gallstone could not be used as index of the environmental contamination, because of the variety on its components.

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